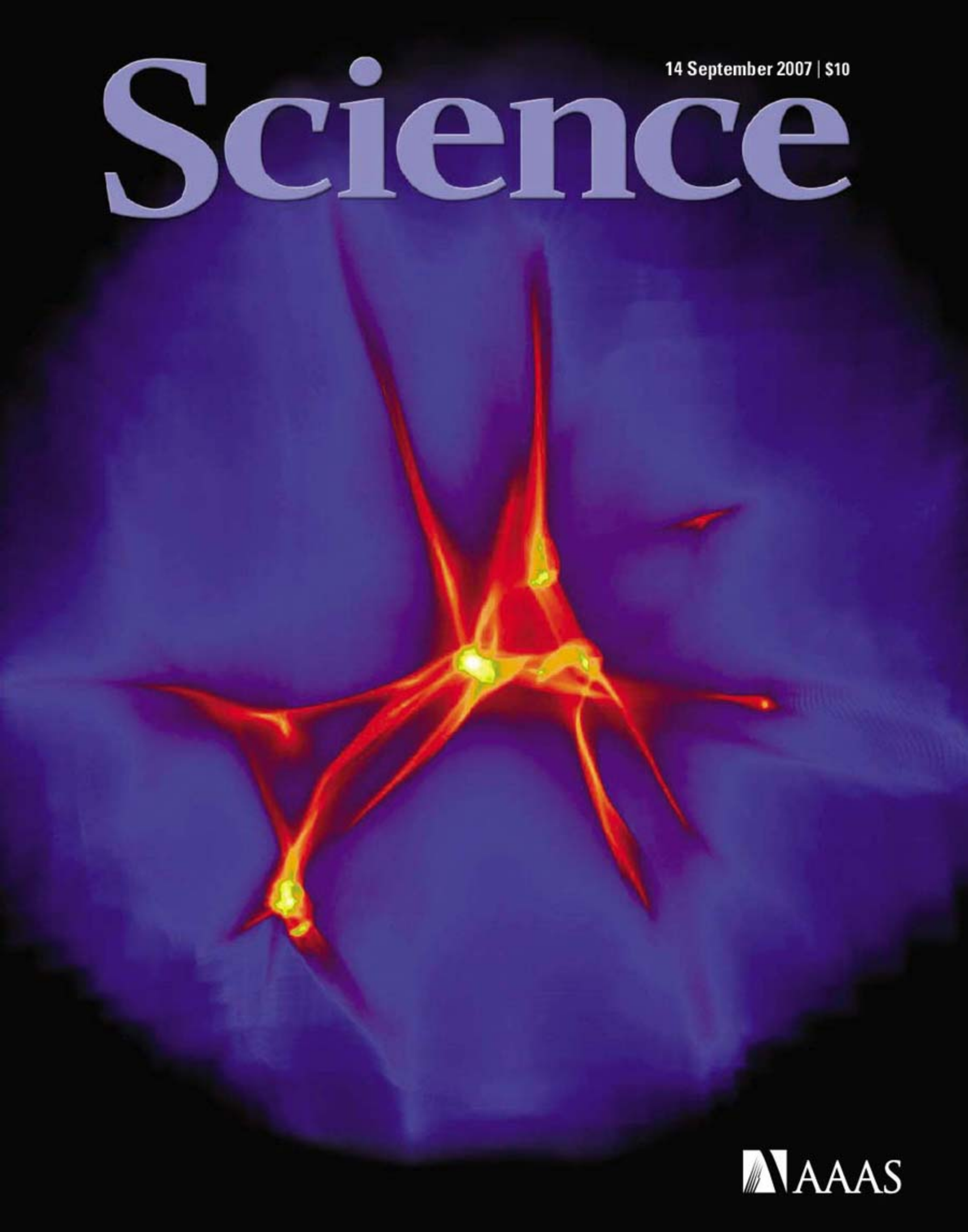
14 September 2007 | $10

Science



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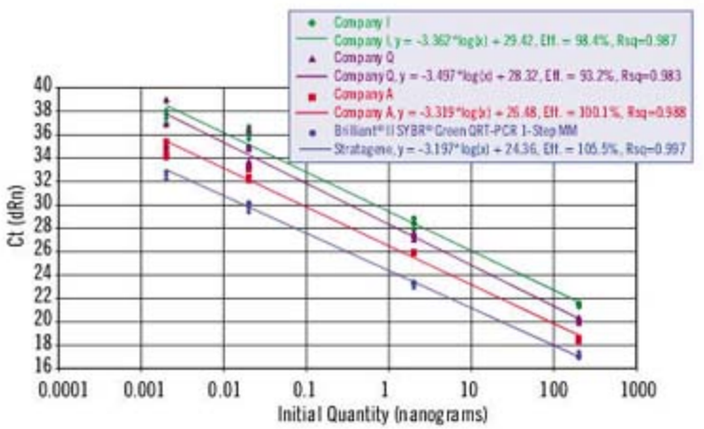

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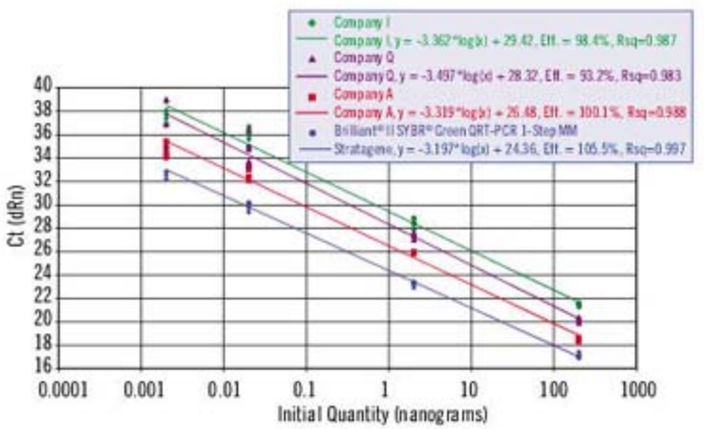

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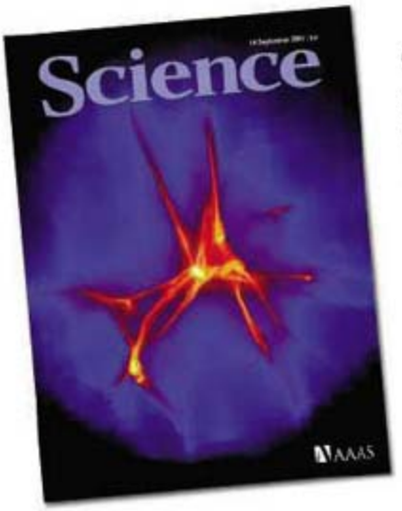

COVER

Supercomputer simulation of the filamentary environment in which the very first stars formed, 100 million years after the Big Bang. The filaments, about 9000 light-years in length, are characteristic of a model universe in which the dark matter consists of fast-moving elementary particles. See page 1527.

Image: Liang Gao and Tom Theuns, Institute for Computational Cosmology, Durham University

DEPARTMENTS

EDITORIAL

NEWS OF THE WEEK

NEWS FOCUS

LETTERS

BOOKS *ET AL.*

POLICY FORUM

PERSPECTIVES

CONTENTS continued >>

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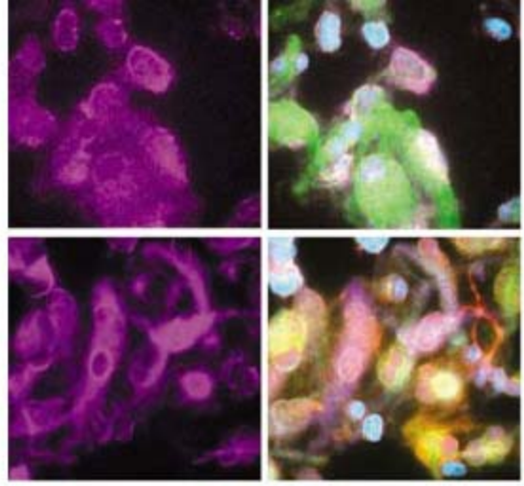


SCIENCE EXPRESS

www.sciencexpress.org

PLANT SCIENCE

FKF1 and GIGANTEA Complex Formation Is Required for Day-Length Measurement in *Arabidopsis*

M. Sawa, D. A. Nusinow, S. A. Kay, T. Imaizumi

Flowering is triggered only when both light and enough of a particular protein are available in the afternoon, conditions only satisfied during longer days of spring.

10.1126/science.1146994

GEOCHEMISTRY

Mass-Dependent and -Independent Fractionation of Hg Isotopes by Photoreduction in Aquatic Systems

B. A. Bergquist and J. D. Blum

The odd isotopes of mercury are fractionated in a mass-independent manner during photoreduction, providing a tracer of mercury species and reactions through food webs.

10.1126/science.1148050

MEDICINE

Coactivation of Receptor Tyrosine Kinases Affects the Response of Tumor Cells to Targeted Therapies

J. M. Stommel et al.

In glioblastoma cancer cells, drugs that work by inhibiting receptor tyrosine kinases are more powerful in combination than when administered as single agents.

10.1126/science.1142946

TECHNICAL COMMENT ABSTRACTS

CANCER

REVIEW

ECOLOGY

1518

BREVIA

DEVELOPMENTAL BIOLOGY

Transplantation of trout spermatogonia to newborn sterile salmon results in male and female adults that produce trout offspring, a method that may help revive extinct species.

RESEARCH ARTICLES

COMPUTER SCIENCE

A series of up to 200 computers running since 1989 has considered the 5×10^{20} possible positions for checkers, showing that perfect play always leads to a draw.

IMMUNOLOGY

An innate immune receptor in humans selectively protects against severe infection of the central nervous system by herpes simplex virus 1.

REPORTS

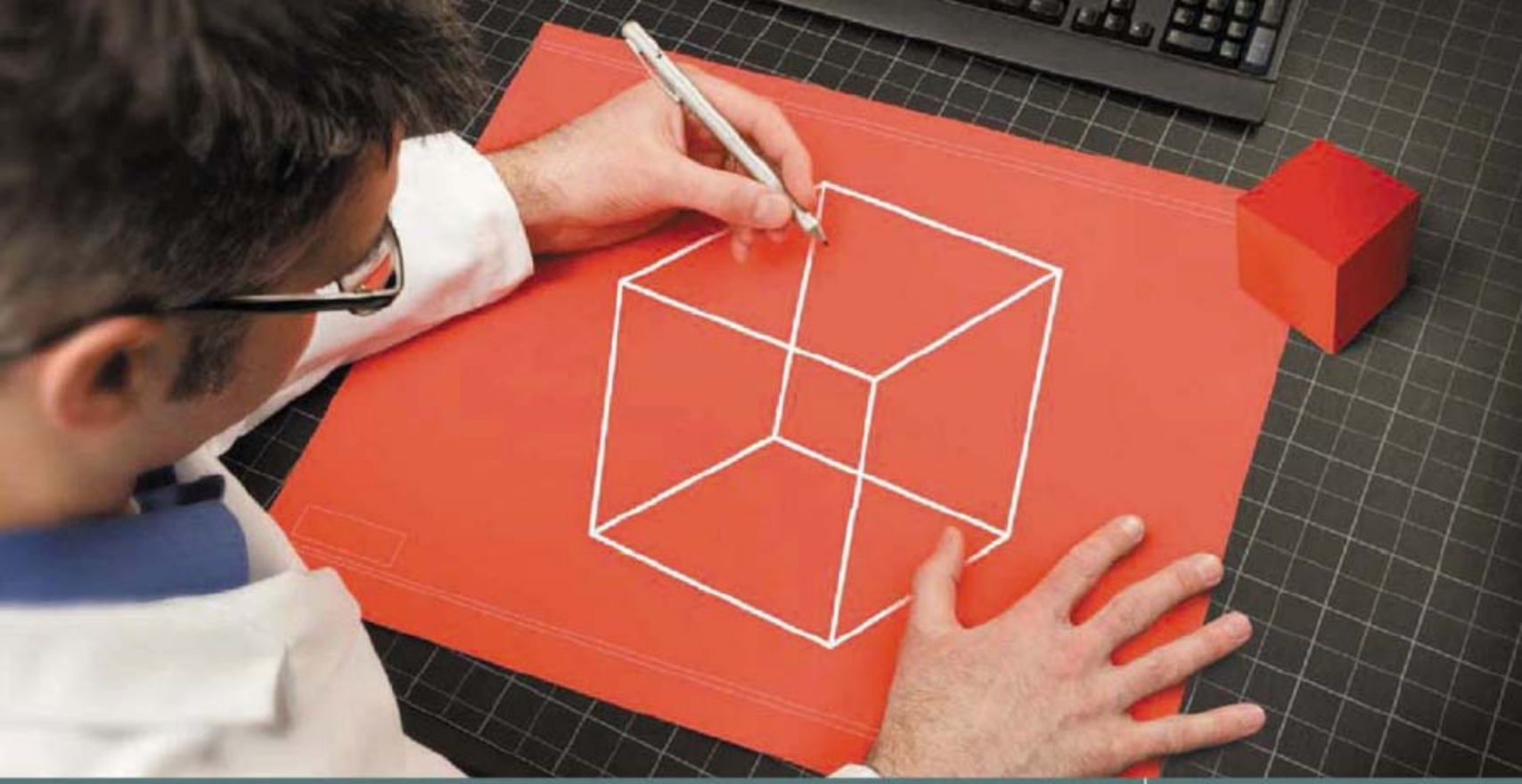
ASTROPHYSICS

In a model of the early universe with warm dark matter, the first stars form in long filaments, not clumps; thus, the star distribution may reveal the dark-matter content. >> *Perspective p. 1511*

PHYSICS

Graphene acts as a quantum billiard table, the edges of which scatter the wave functions of electrons and holes, producing interference effects that depend on the sheet geometry.

CONTENTS continued >>



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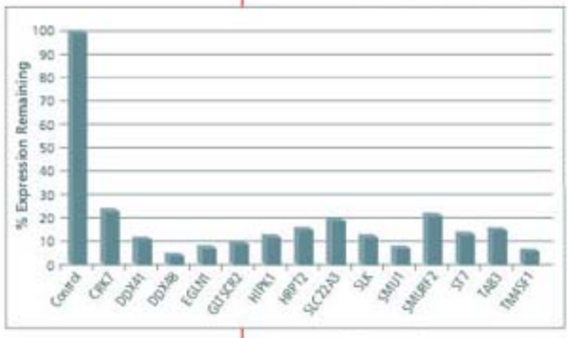

Silencing efficacy of representative MISSION siRNAs designed using the Rosetta algorithm. Target mRNA levels were measured by the QuantiGene® Reagent System from samples harvested 24 hours after transfection into HeLa cells.

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REPORTS *CONTINUED...*

1507 & 1554

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CONTENTS continued >>

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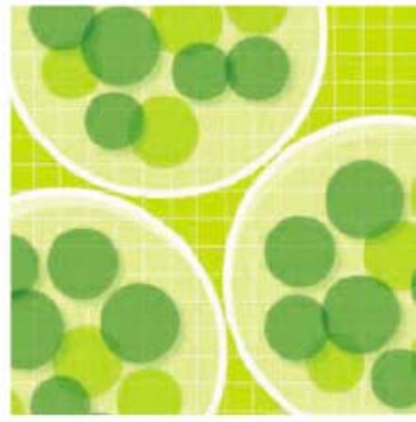

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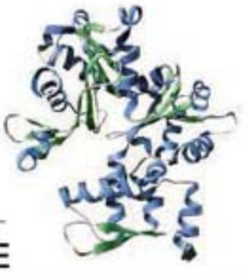
Gray Whales Far From Recovered?
Genetic analysis reveals population is still well below its historic high.

Born to Run Long Distance
Stamina-stretching mutation widespread in some groups of people.

Dwindling Days for Arctic Ice
New projections suggest greater and greater annual melts.



β-actin, a regulator of nitric oxide synthase.

SCIENCE'S STKE

www.stke.org SIGNAL TRANSDUCTION KNOWLEDGE ENVIRONMENT

PERSPECTIVE: Dialog Between LKB1 and AMPK—A Hot Topic at the Cellular Pole
C. Forcet and M. Billaud
LKB1 appears to be a novel class of tumor suppressor that acts as an energy-sensing and polarity checkpoint.

PERSPECTIVE: β-Actin—A Regulator of NOS-3
Y. Su, D. Kondrikov, E. R. Block
β-actin regulates the activity of nitric oxide synthase type 3 directly and indirectly through Hsp90.

SCIENCE CAREERS

www.sciencecareers.org CAREER RESOURCES FOR SCIENTISTS

GLOBAL: Should I Do a Ph.D.?
E. Pain
Whether or not to do a Ph.D. is a decision many students blindly undertake.

US: Opportunities—The Most Important Venture Capitalist
P. Fiske
Uncle Sam may be the key venture capitalist to help start your science-based company.

US: A New Tech Nexus in Silicon Valley
A. Fazekas
The Bio-Info-Nano Research and Development Institute will do research and train scientists.

US: From the Archives—Facing Life's Challenges as a Foreign Scientist
X. Huang
Postdoc Xinyan Huang overcame many obstacles when she first arrived as a student from China.

SCIENCEPODCAST

Download the 14 September *Science* Podcast to hear about modeling cultural conflict, circadian clocks and mental health, early star formation, and more.
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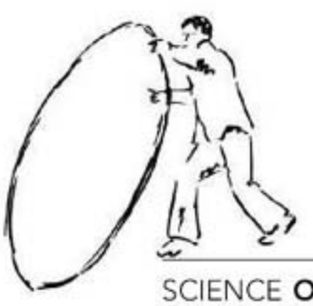

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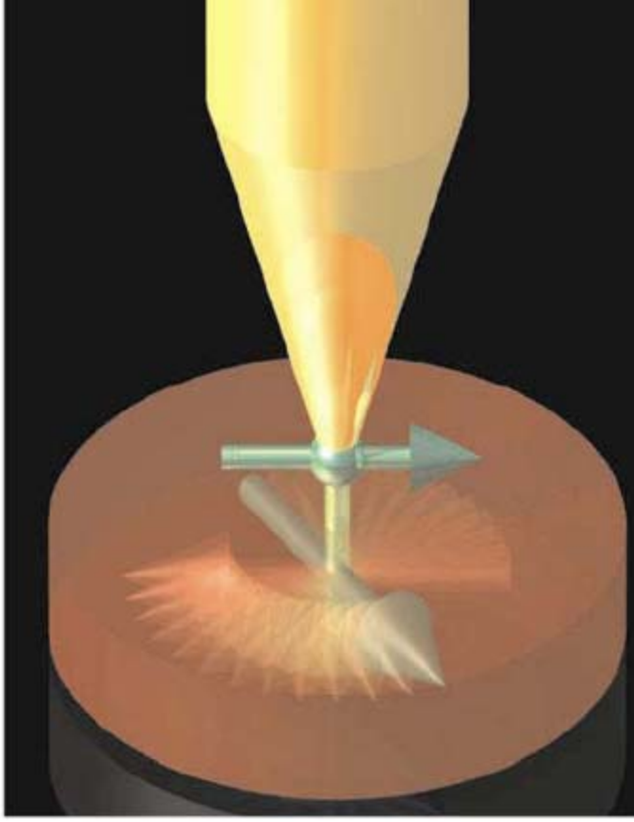


<< Switching Magnetism on the Spot

In magnetic hard drives, information is typically written by application of a magnetic field, and readout is performed with a separate electrical probe. The bit densities that can be achieved this way are limited by stray magnetic fields that can affect nearby bits and possibly destroy information that was already stored. The use of spin-polarized current to locally control and read out the magnetization is expected to overcome such problems, but the underlying mechanisms involved in spin-polarized magnetization switching remain unclear. **Krause *et al.*** (p. 1537) show that spin-polarized current from a scanning tunneling microscope tip can be used to both manipulate and read out the magnetization in small islands of iron atoms. The magnetization switching in the island is dominated by a spin-torque effect exerted by the spin-polarized current, whereas the Oersted field (magnetic field arising from current flow) is small.

A No-Win Solution for Checkers

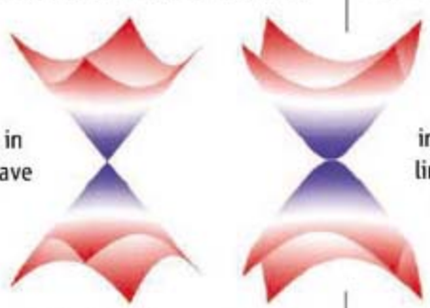
Computer scientists have traditionally used games such as chess as test cases for research in artificial intelligence. Less challenging games that have a small search space can be completely solved with computers by examining every possible set of moves from a given starting position. Chess has an immense search space that would require the fastest computers eons to solve, but other games provide tough but feasible challenges. **Schaeffer *et al.*** (p. 1518, published online 19 July; see the 20 July news story by **Cho**) report their solution of the game of checkers. If black moves first, and the opponents execute perfect play, the game ends in a draw. The analysis began in 1989 and required dozens of computers for a complete solution.

Strings of Stars

Gravity caused the first stars that formed in the early universe to collapse in overly dense regions. These regions were seeded by clumps of dark matter, particles that neither glow nor interact with light except gravitationally. Most modeling of the first stars has used "cold" dark matter, but it is possible that the dark matter was "warm" if it was made of more energetic fundamental particles. In computer simulations that include warm dark matter, **Gao and Theuns** (p. 1527, see the cover and the Perspective by **Bromm**) show that the faster motions of the warm dark matter erased very small density structures, and quite stable elongated gas clouds formed instead that fragmented to produce strings of stars. Thus, the pattern of the first stars may tell us about the dark matter content of the universe.

Graphene Billiards

With its distinctive band structure and mechanical stability, graphene (isolated sheets of graphite) has been predicted to exhibit a number of exotic transport properties. However, the transport of carriers around the Dirac point (where the electronic bands meet in momentum space) that gives rise to many of the predicted properties has remained controversial. **Miao *et al.*** (p. 1530) systematically studied transport properties around this region in device structures of various sizes in which the carrier densities could be varied. Carriers in the graphene have a large coherence length that causes its transport to depend on geometry. In effect, the wave functions of electrons and holes can interfere as they are scattered from the edges of the graphene sheet, which acts like a quantum coherent billiard.



Pass the Sulfur, Please

Carbon and sulfur isotopic signatures provide the main evidence for the identification of the earliest life on Earth. Details in the signatures of the several sulfur isotopes can now be used to track metabolism. It was previously suggested that a large fractionation in the ^{34}S versus ^{32}S isotopes implies that sulfate-reducing bacteria were present in rocks dated to about 3.5 billion years ago. **Philippot *et al.*** (p. 1534; see the Perspective by **Thamdrup**), making use of ^{33}S data, show these rocks record the presence of organisms that metabolized and disproportionated elemental sulfur. Several such organisms are present near the base of the phylogenetic tree.

Human Interactions

Humans have continuously interacted with natural systems. **Liu *et al.*** (p. 1513) review the intricate nature of the organizational, spatial, and temporal couplings of human and natural systems. Case studies on different continents suggest that couplings have evolved from direct to more indirect interactions, from adjacent to more distant linkages, from local to global scales, and from simple to complex patterns and processes. An appreciation of such interactions should help in the development of effective policies for ecological and socioeconomic sustainability. Humans not only interact with nature but with one another in groups. **Lim *et al.*** (p. 1540) have adapted concepts of phase separation familiar in chemistry and physics to study patterns in global populations that can help predict and perhaps prevent conflicts. They posit that violence arises at boundaries between regions that are not sufficiently well defined. A model based on spatial distributions of ethnic groups gave good predictions about regions of violence in the former Yugoslavia and in India.

Continued on page 1467

CREDITS (TOP TO BOTTOM): STEFAN KRAUSE/UNIVERSITY OF HAMBURG; MIAO *ET AL.*

Continued from page 1465

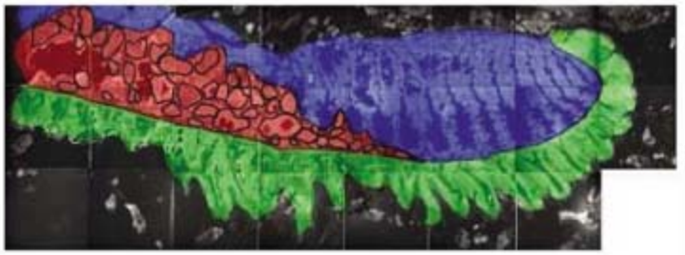
Tailor-Made Toll-Like Receptor

Laboratory-based immunology has revealed much about the role of innate immune receptors from insects to mammals, but to what extent do such receptors protect humans from infections? **Zhang *et al.*** (p. 1522) report a primary human immunodeficiency that points to a dedicated role for a Toll-like receptor (TLR) in protection from infection with a single specific virus, without any apparent influence on other pathogens. Herpes simplex virus (HSV) causes encephalitis in children carrying a mutant allele of TLR3, which normally regulates the antiviral interferon response to virus nucleic acid in the central nervous system and in dendritic cells of the immune system. Maintenance of TLR3 in the innate armory of humans may have been driven by viral infection. These results suggest that other similarly narrow host-pathogen interactions may have also co-evolved.

Functional Evolution of Proteins

The direct identification of protein evolution mechanisms requires comparing proteins through evolutionary time. The sequence of the 450-million-year-old ancestor of vertebrate mineralocorticoid (MR) and glucocorticoid (GR) was previously determined by phylogenetic analysis, and the ancestor was shown to have MR-like hormone specificity. **Ortlund *et al.*** (p. 1544, published online 16 August; see the 17 August news story by **Service**) used structural, functional, and phylogenetic analysis to determine how specific mutations resulted in a change from MR-like to GR hormone specificity. They find evidence for epistatic interactions where a substitution changed the conformation at another site. Substitutions that had no immediate functional effect, but affected stability to allow subsequent functional switching mutations, played an important role in GR evolution.

An Airy Meal



The fixation of atmospheric nitrogen into ammonia that is essential to human nutrition and global ecosystems is performed by free-living bacteria and by symbionts in plant root nodules. **Lechene *et al.*** (p. 1563; see the Perspective by **Kuypers**), using multi-isotope imaging mass spectrometry with the stable isotope of ^{15}N, measured nitrogen fixation by symbiotic bacteria. They traced the utilization of fixed nitrogen, in this case by animal rather than by plant host cells.

Doubling Up Antibody Specificity

The light and heavy chains that make up antibodies both carry variable regions at their ends that combine to form the highly diverse antigen-binding sites of the antibody molecule. Immunological dogma states that a single B cell generates antibodies of one defined specificity (each molecule carries identical, symmetric heavy-light chain combinations), but one particular class of antibody known as immunoglobulin G4 (IgG4) has been suspected of breaking this rule. **Van der Neut Kolfschoten *et al.*** (p. 1554; see the Perspective by **Burton and Wilson**) now provide direct evidence that IgG4 can swap a heavy-light combination on one fragment antigen-binding arm for another, which creates antibodies with dual specificity. Furthermore, in a model of disease that relies on cross-linking by antibodies, the loss of single specificity (and the loss of the ability to cross-link) was effective at reducing disease.

Regulatory Motifs in Making Muscle

During metazoan development, multiple genes are co-expressed so that interacting gene products can be produced in the same place and time. **Brown *et al.*** (p. 1557) examined how genes that function together are coordinately expressed by dissecting cis-regulatory elements in 19 co-regulated *Ciona* genes that encode components of a muscle multiprotein complex. Assays defined the cis-regulatory elements through mutational analyses, and mutant-construct gene expression in muscle cells was quantified to estimate the activity of each regulatory motif. A comparison between the divergent species *C. intestinalis* and *C. savignyi* revealed that motif arrangements differ widely among co-regulated genes within a species but orthologous motifs are evolutionarily conserved.

CREDITS (TOP TO BOTTOM): LECHENE *ET AL.*

Anita K. Jones is a professor in the Department of Computer Science at the University of Virginia, Charlottesville, VA, and chaired the National Academies committee that produced the report *Polar Icebreakers in a Changing World: An Assessment of U.S. Needs*.

An Icy Partnership

KNOWLEDGE OF THE WORLD'S POLAR REGIONS—ANTARCTICA AND THE ARCTIC—IS OF international interest for economic, environmental, territorial, and security reasons. Studying these environments has been a cooperative activity among countries for half a century. Icebreaker ships have played a critical role. Unfortunately, the U.S. icebreaking capability has deteriorated substantially. Of the world's roughly 50 high-capability icebreakers (at least 10,000 horsepower and capable of steaming steadily through ice 4 to 8 feet thick), Russia possesses 15. Canada operates six. The U.S. government owns three, two of which are at the end of their 35-year service lives. This not only threatens U.S. access to these regions but also jeopardizes the ability of the U.S. research community to conduct solo and international research missions. A long-lived successful partnership between the polar research community and the U.S. Coast Guard (USCG), which operates the government icebreakers, has been built over decades. That partnership is unhealthy now and should be revitalized.

Many nations have benefited from the knowledge gained from research in both polar regions. For example, we have a deeper understanding of the molecular mechanisms that animals use to cope with freezing conditions, the transport of organic pollutants to polar food webs, and the influence of the polar regions on the deep ocean "conveyer belt."

Eight nations (Canada, Denmark, Finland, Iceland, Norway, Sweden, the Russian Federation, and the United States) have land and population in the Arctic. Their interests are not only scientific but also encompass security, law enforcement, environmental, and economic matters. With increased retreat of the summer ice margin, human activity, especially that related to resource exploitation, is likely to increase. The Russians (only) have made a territorial claim to about half of the seabed under the Arctic Ocean. Other nations are considering their response to the Russian flag recently planted at the North Pole.

Increased human activity in the Arctic necessarily requires an increased presence in ice-bound waters. The U.S. has combined USCG Arctic patrols for maritime and environmental safety and maritime law enforcement with research cruises. Building or contracting for separate ships for the two missions is less cost-effective, particularly for the research community. Past history shows that the missions and objectives of the research community and the USCG are compatible, even complementary. These can be simultaneously served by an icebreaker following a course suitable for research by 30 to 50 scientists aboard.

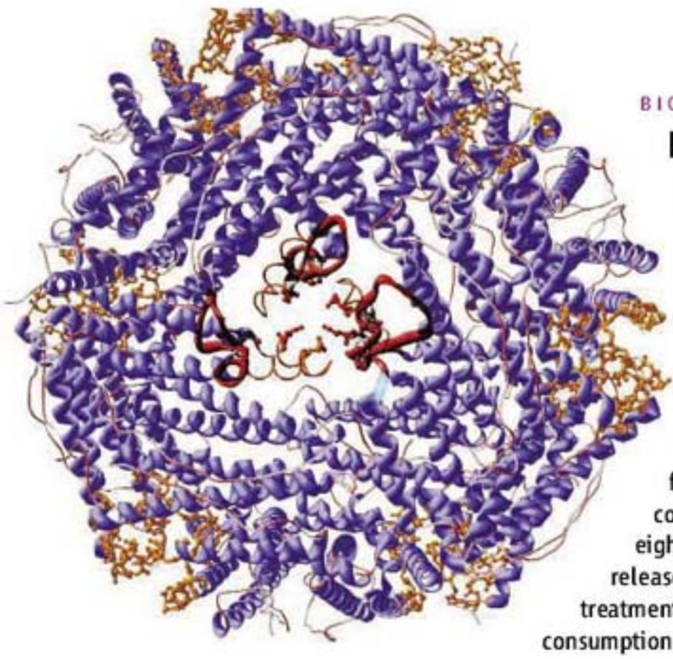
The fracture in the USCG/scientific community partnership comes from the Coast Guard's inability to fund replacements for the aging icebreaker ships. Surprisingly, the U.S. Office of Management and Budget (with congressional concurrence) transferred the budget for operating icebreakers to the National Science Foundation (NSF), a major funder of polar research. As a result, a science agency is currently making decisions that affect the safety and training of a military force, risking NSF's reputation and posing potential physical dangers to the crew. Until the fleet's recent deterioration, the USCG icebreaker ships made an annual break-in to McMurdo Station in Antarctica, so that tanker and cargo ships could provision research activity. In recent years, NSF has contracted for ships from other nations to do the annual break-in, but those ships have not always performed without incident.

In 2004, Congress asked the National Academies to investigate what icebreaking capability the United States needs and how best to acquire and operate that capability. Our committee reaffirmed the value and efficacy of the USCG/research community partnership and recommended replacing the aging icebreakers with new ships, designed with research community involvement. Modern technology, particularly for hull design, propulsion, and electronics, can deliver vessels to support needs in the Arctic and Antarctic without increasing the current number of ships. The Coast Guard should be funded to build and operate the new ships. Researchers should pay the modest incremental costs incurred by their presence on a cruise, as in the past. This would revitalize the decades-old icy partnership that benefits not only U.S. interests but also the world community of polar researchers.

– Anita K. Jones

10.1126/science.1149334

CREDIT: JOSH LANDIS/NATIONAL SCIENCE FOUNDATION



BIOCHEMISTRY

Peptides to Sway Iron Levels

Ferritin proteins are best known for storing iron within their cores, but ferritins also release iron when it is needed, such as during hemoglobin synthesis or when iron is lost through hemorrhage. Although the release process is driven by the reduction of Fe^{3+} and uptake by Fe^{2+} chelators or chaperones, changes in the gated pore of the protein, such as mutations of conserved pore residues, affect the rate of iron release, and in vitro, millimolar concentrations of urea can unfold pore helices and increase the release rate. Liu *et al.* searched a combinatorial peptide library of ferritin-binding peptides and identified a single heptamer that accelerated iron release threefold, and when combined with Desferal, an iron chelator in therapeutic use, led to an eightfold increase. Another heptapeptide was identified that decreased iron release, possibly by binding across the pore. Potential applications include treatment of iron overload or limiting unwanted effects of iron release, such as consumption of cellular reductants. — PDS

J. Biol. Chem. **282**, 10.1074/jbc.C700153200 (2007).

APPLIED PHYSICS

Sending Plasmons Round a Bend

The orders-of-magnitude size difference between optical fibers and nanometer-scale electronic circuitry presents a substantial compatibility gap between the fast long-distance optical signal communications offered by photonics and the convenience of small-scale integrated microelectronics. Surface plasmons are hybrid excitations of light and packets of electrons confined to the interfacial region of a metal and a dielectric, and they offer the potential to fill that gap. However, plasmons are dispersive and tend to leak away because of scattering and radiation losses, giving rise to the general problem of efficiently guiding the plasmons around the two-dimensional plane to desired sites. Steinberger *et al.* have fabricated surface plasmon waveguides by lithographically patterning tracks of silicon dioxide deposited on a gold film. They demonstrate the ability to guide plasmons around a 90° bend, showing that there is a tradeoff between bend radius and propagation length for the optimal transmission of the plasmons through the waveguide. The results should help shrink the incompatibility gap yet further. — ISO

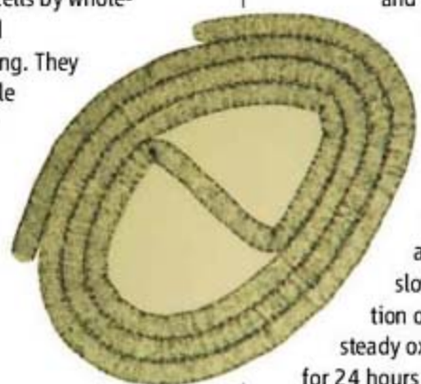
Appl. Phys. Lett. **91**, 81111 (2007).

BIOCHEMISTRY

Mobile Electron Carriers

Microbes that have not yet been cultured under laboratory conditions are, not surprisingly, rather more difficult to work with than those that have, such as the perennial workhorses *Escherichia* and *Saccharomyces*. Nevertheless, recent forays into soil and marine communities have hinted at a wealth of untapped pharmaceutical and biochemical expertise, and technological advances in extracting and sequencing genomic DNA of unpurified (and in many cases, unseen) organisms have begun to bring those microbial skills within reach.

Mußmann *et al.* have analyzed a single *Beggiatoa* filament (roughly 30 μm wide and 1 cm long) of almost 1000 cells by whole-genome amplification and pyro(phosphate) sequencing. They have been able to assemble enough sequence to cover approximately ¾ of the 11-Mb genome as estimated by the recovery of single-copy marker genes and aminoacyl tRNA synthetases. The collection of sulfur-, nitrogen-, and oxygen-metabolizing enzymes, albeit still incomplete, provides genetic evidence for the elevatorlike lifestyle of this bacterium, which cycles vertically as it harvests energy from the oxidation of sulfidic deposits. At the relatively oxygen-rich surface of marine sediments, electrons from elemental sulfur are donated to oxygen, yielding sulfate; in deeper, anoxic regions of the sediment, nitrate is recruited as the acceptor of electrons from hydrogen sulfide. *Beggiatoa* are energetic hoarders of nitrate, accumulating it in vacuoles in concentrations as high as 0.5 M to the dismay of competing denitrifying bacteria. — GJC



Beggiatoa filament.

PLoS Biol. **5**, e230 (2007).

MATERIALS SCIENCE

Oxygen on Demand

In the design of artificial tissues or repair of large wounds, one critical limiting factor is the availability of the oxygen necessary for vascularization and healing to occur. To skirt slow oxygen diffusion, Harrison *et al.* have explored the possibility of creating a material that can generate oxygen in situ. Sodium percarbonate was mixed with poly(D,L-lactide-*co*-glycolide) (PLGA) in solution, and films were solution-cast and slowly dried to prevent the formation of voids. In a moist environment, steady oxygen production was observed for 24 hours and then gradually slowed and ended after 70 hours in total. PLGA films were placed under dorsal skin flaps in mice and then observed over a period of 1 week. Those containing sodium percarbonate exhibited a significant decrease in flap necrosis over the first 3 days, along with less visible tissue damage and greater mechanical strength. However, there was no benefit after a week in comparison with untreated PLGA films. The authors are seeking to extend the oxygen release time, either through encapsula-

Continued on page 1473

CREDITS (TOP TO BOTTOM): LIU ET AL., *J. BIOL. CHEM.* **282**, 10.1074/JBC.C700153200 (2007); MUßMANN ET AL., *PLOS BIOL.* **5**, E230 (2007)

Continued from page 1471

tion of the sodium percarbonate or through the use of different oxygen-generating chemical components. — MSL

Biomaterials **28**, 4628 (2007).

CHEMISTRY

Breaking Two Rings

Polyesters have traditionally been prepared by condensation of monomers bearing acid or ester groups: The chain grows by formation of O-C bonds with concomitant loss of water or alcohol. Choosing a cyclic monomer can eliminate formation of these small-molecule by-products, as chain growth proceeds by ring-opening, but this approach offers limited functional diversity along the polymer backbone. Jeske *et al.* have developed a zinc catalyst that links epoxides to cyclic anhydrides through alternating ring-opening steps and thereby introduces backbone substituents ranging from methyl and cyclohexyl to vinyl moieties by appending them to the strained three-membered rings. A cyano group on the diiminate ligand coordinated to zinc proved key to catalyst stability under the reaction conditions. The system achieved number-average molecular weights exceeding 10^4 and low polydispersities (1.1 to 1.5). — JSY

J. Am. Chem. Soc. **129**, 10.1021/ja0737568 (2007).

PSYCHOLOGY

Pressure From Above

A recent interdisciplinary trend is the use of economic transactions, which yield a quantitative expression of preferences, in experimental studies of human social behavior. In the anonymous one-shot dictator game, a person is allotted the task of taking any part or all of a sum of money, with the remainder given to a second person who is neither seen nor encountered again. Shariff and Norenzayan engaged 75 residents (ages 17 to 82) of Vancouver and offered them the opportunity of playing this game after having completed one of three possible scrambled sentence tests. Across the three groups, the modal choice was to take either the entire amount or only half of it. Within each of the two groups who had been implicitly primed with concepts of religion or of civic justice, 11 out of 25 people ceded half of the money, as compared to 10 of 25 absconding with everything in the neutral prime condition. Furthermore, both types of pro-social priming evoked significantly greater expressions of generosity (than the neutral prime) by theists. Linking institutional systems of morality to other-regarding behavior by individuals lends support to the proposal that the development of social norms enabled the increase of group size in our human ancestors. — GJC

Psychol. Sci. **18**, 803 (2007).

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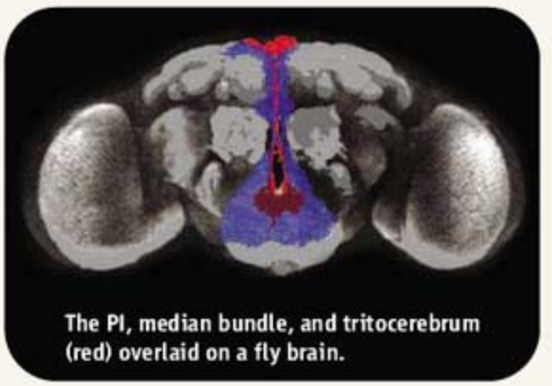
<< Knitting a Ravelled Sleave

For an activity in which we spend a third of our lives, much about sleep remains enigmatic. Foltenyi *et al.* investigated the role of epidermal growth factor receptor (EGFR) signaling in regulating sleep in *Drosophila*. In the fly, the activation of EGFR ligands such as Spitz depends on the transmembrane protein Star and on Rhomboid family (Rho) proteases. Using flies in which Rho and Star expression could be conditionally induced, they showed that overexpression led to a transient increase in both the duration and number of sleep episodes, which was followed by a decrease and then a return to normal. The overexpression of Rho and Star also led to an increase in phosphorylation of extracellular signal–regulated kinase (ERK, a target of EGFR signaling) that paralleled the temporal pattern of increased sleep, and the increase in ERK phosphorylation was greatest in the tritocerebrum. Moreover, several lines of flies in which Rho activity in neurons projecting from the pars intercerebralis (PI, a region analogous to the vertebrate hypothalamus) to the tritocerebrum was inhibited with RNA interference showed decreased sleep. This decrease involved brief sleep episodes in conjunction with an increase in the number of times that sleep was attempted—potentially a fly model of insomnia. The authors propose that the production of EGFR ligand by PI neurons leads to ERK activation in tritocerebrum neurons, thereby promoting sleep. — EMA

Nat. Neurosci. **10**, 1160 (2007).



The PI, median bundle, and tritocerebrum (red) overlaid on a fly brain.

CREDIT: FOLTENYI ET AL., NAT. NEUROSCI. 10, 1160 (2007)

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NET WATCH

Down in the Swamp

"The Ever Glades [*sic*] are now suitable only for the haunt of noxious vermin, or the resort of pestilent reptiles." That was the verdict of an 1848 report to Congress that recommended draining the vast Florida wetland. It's one of the jewels tucked away in the Everglades Digital Library, created by Florida International University in Miami.

The archive contains more than 400 articles, maps, photos, and other materials about south Florida's history and environment. Offerings range from plant censuses and rainfall analyses to recorded interviews with Marjory Stoneman Douglas (1890–1998), the writer who galvanized efforts to preserve the Everglades. In this 1908 photo, a girl in Miami poses on a stuffed alligator. >>
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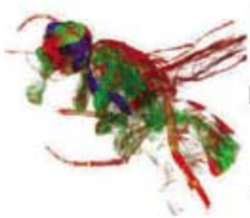
Psyching Out the Fruit Fly

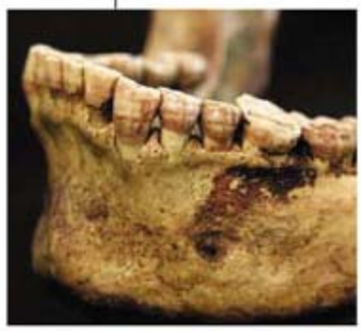
Fruit fly brains are useful for studying genes implicated in neurological disorders such as Alzheimer's and Parkinson's disease. Getting at them, however, requires messy dissections that can damage tissue. Now, a new technique may offer a hands-off peek into the miniature mind of *Drosophila*.



A team led by Leeanne McGurk of the Medical Research Council's Human Genetics Unit in Edinburgh, U.K., takes flies bred with genetic markers that make the nervous systems fluoresce (blue, in photo) and bleaches their exoskeletons, making the bodies translucent. Optical projection tomography reveals the 3D structure of the organs and allows researchers to virtually slice the flies' brains on any axis, the authors report online on 5 September in *PloS One*. The procedure may one day be automated, collaborator Liam Keegan says, and—with better resolution and longer-lived fluorescence—could make hand-dissection of fruit fly brains a thing of the past.

Farming Good For Health

The worldwide agricultural revolution that began about 10,000 years ago had its downside: Many researchers have found that early farmers were not as healthy as their hunter-gatherer ancestors (*Science*, 9 June 2006, p. 1449). But a new study of teeth from Nile Valley farmers offers the first comprehensive evidence—from data spanning some 10,000 years—that the farming life was better for health in the long run.



Teeth from an early Neolithic farm woman show enamel loss.

Childhood exposure to stress from disease or bad nutrition has a lasting effect on the formation of tooth enamel. So anthropologists Anne Starling of Duke University in Durham, North Carolina, and Jay Stock of the University of Cambridge in the U.K. studied the teeth of 242 individuals who lived in the Nile Valley between 13,000 and 1500 B.C.E. They found that 70% of the Badari people, early farmers who lived between 5000 and 4000 B.C.E., showed signs of enamel loss, compared to only 39% of hunter-gatherers from the same area a few thousand years earlier. But once food stocks became more reliable, health improved markedly: Only 33% of people who lived from 4000 to 3100 B.C.E. had lost enamel. And by 2000 B.C.E., the incidence was down to 21%, the authors reported online 4 September in the *American Journal of Physical Anthropology*.

Anthropologist Clark Larsen of Ohio State University in Columbus calls the study "especially interesting" because it shows that health improved with the rise of urbanization and the Egyptian state. He also says it bolsters the notion that hunter-gatherers were initially pushed into farming by population pressures or climate changes.

Bear Facts

Why does a bear rub in the woods? This giant grizzly bear from the forests of British Columbia had his tree-rubbing habits scrutinized as part of a project to get to the bottom of the question. It seems that bears engage in scent marking, rubbing, biting, and scratching the same trees over many seasons. Once a bear has "anointed" a tree, others follow suit—in fact, stepping in the same tracks.

To learn more, Owen Nevin, now at the University of Cumbria in Wales, set up cameras in four bear-rubbing trees and recorded 52 bear events on spring nights in 2005 and 2006. It's mainly adult males that do it, Nevin reported this week at a British Ecological Society meeting in Glasgow, U.K. He says the evidence suggests that dominant males use tree marking to warn off or override the scent of competitors for both territory and females.

It's an unusually thorough experiment, says Barrie Gilbert, who was Nevin's graduate adviser at Utah State University, Logan. But there are still a lot of unknowns—such as why bears choose the trees they do.

CREDITS (TOP TO BOTTOM): HISTORICAL MUSEUM OF S. FLORIDA; JAY STOCK/LCHES; O. NEVIN; LEEANNE MCGURK AND MARY O'CONNELL

RISING STARS

WELL-CONNECTED. Most people owning a phone that doesn't work with their family's T-Mobile service plan would either switch providers or get a different phone. Not George Hotz, who spent the summer after his high school graduation from Bergen County Academies in New Jersey finding a way to unlock his iPhone from the device's sole service provider, AT&T. Hotz posted his solution, which involves altering the phone's circuit board and uploading unique programs, on his blog 23 August before heading off last week to begin classes at the Rochester Institute of Technology in New York state.

The rewired iPhone isn't Hotz's first technological triumph: In May, he was a top finisher in the 2007 Intel International Science and Engineering Fair for a spinning computer display capable of creating 3D images.

Hotz reports that he traded one unlocked phone for more iPhones and a "sweet Nissan 350Z," which lists new starting at $27,900. And the phone in his pocket is working fine.

POLITICS

JUMPING IN ... Bill Foster (right) spent 22 years as an experimental physicist at Fermi National Accelerator Laboratory in Batavia, Illinois. Now he wants to set up shop in the U.S. Congress. He's running for the seat being vacated by the former House Speaker, Illinois Republican Dennis Hastert, who is retiring next year.

A Democrat and a fellow of the American Physical Society, the 51-year-old Foster says Congress needs more members with a scientific background. "Almost every issue we face has a technical edge," he says. "To get good policy, you need clear goals, a good technical understanding, and a firm grasp of economics." Foster says he would push for more research into biofuels, participation in international efforts to fight climate change, and a renewed emphasis on nuclear nonproliferation.

Observers say Foster's deep pockets should serve him well in his campaign. As teenagers, he and his brother Fred started a company that now makes most of the theater lighting in the United States. "He's a serious candidate because he has vowed to spend at least $1 million of his own money," says Eric Krol, a political writer for the local *Daily Herald*. But although Foster may outspend his two Democratic rivals, Republican businessman Jim Oberweis plans to spend $2.5 million on his campaign, and, Krol notes, the district is "still one of the more Republican parts of Illinois."

... BOWING OUT. Peter Agre, the Nobelist in chemistry who dreamed of becoming a senator, has decided after dipping into Minnesota's politics that the waters are too chilly for him. Agre, 58, took leave from his job as vice chancellor for science at Duke University in Durham, North Carolina, to see if he could stir up enough enthusiasm—and cash—for a run next year against the incumbent senator, Republican Norm Coleman (*Science*, 25 May, p. 1112).

To his dismay, says Agre, an outspoken liberal, the main obstacle was not conservative opposition but an inability to impress the Democratic Party, whose help he needed: "There's a huge priority on how much money you can raise; ... [party leaders] were looking for at least $10 million." He says having two rich Democrats already in the field—comedian Al Franken and attorney Michael Ciresi—also put a damper on his plans.

Got a tip for this page? E-mail people@aaas.org

CREDITS (TOP TO BOTTOM): ROCHESTER INSTITUTE OF TECHNOLOGY; BILL FOSTER FOR CONGRESS CAMPAIGN; EFA

Three Q's >>

For nearly a decade, **Bernat Soria Escoms**, 56, has been trying to turn embryonic stem cells into insulin-producing cells for treating diabetes, most recently at his lab at the Andalusian Center for Molecular Biology and Regenerative Medicine in Seville, Spain. In July, Spain's President José Luis Rodríguez Zapatero appointed him to join the Cabinet as minister of health and consumer affairs. The ministry, based in Madrid, also controls much of Spain's $2 billion biomedical research budget.

Q: You have said you were surprised by the job offer. Was it a hard decision?
Yes, but if you say no, you can never again criticize the government.

Q: Do you miss your lab?
The Council of Ministers meeting ends at noon on Friday, and I then take the fast train to Seville. I am in the lab Friday afternoon and evening and on Saturday. If the minister of culture goes to exhibitions and the theater [to stay current in the arts], I can go to the lab.

Q: When will stem cell research have a measurable impact on doctors and patients in Spain?
Very soon, if you consider stem cells as a broad concept including adult stem cells. In the coming weeks, I will announce a program for clinical research on cell therapies for 12 diseases, including complications from diabetes, cardiopathy, multiple sclerosis, amyotrophic lateral sclerosis, and muscular dystrophy. For embryonic stem cells, we are still at the level of basic research.

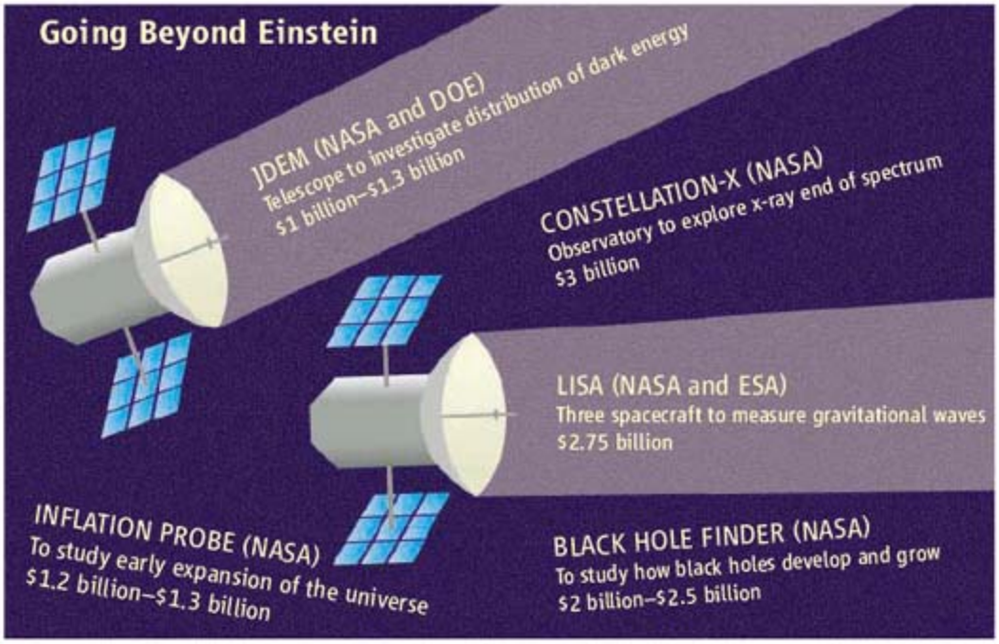
On the critical list 1484

A virus's European toehold 1485

SPACE PHYSICS

Beyond Einstein Should Start With Dark Energy Probe, Says Panel

Dark energy is a subtle force believed to be responsible for accelerating the universe's expansion. Last week, it also proved irresistible to a panel of U.S. physicists and astronomers asked to set priorities for an ambitious set of modestly priced missions to tackle the most exciting cosmological questions of the era. Its report recommends that NASA and the Department of Energy (DOE) begin work next year on a $1-billion-plus Joint Dark Energy Mission (JDEM), while saying that plans for four other space physics spacecraft should be delayed—some indefinitely, given the pressure on NASA's science budget.



In the spotlight. A new report ranks the proposed missions under NASA's Beyond Einstein program and offers cost estimates significantly higher than those from project teams.

Four years ago, cosmologists came up with five distinct projects to examine black holes, gravitational waves, dark matter, the early inflation of the universe, and dark energy as part of what NASA labeled its Beyond Einstein program. Faced with tight budgets and prompted by congressional concerns, the agency last year asked the National Academies' National Research Council (NRC) for advice on deciding which missions should get off the ground first, starting in 2009. The council's 220-page report, issued 6 September, gives top billing to the dark energy effort, followed by the Laser Interferometer Space Antenna (LISA), a three-satellite mission designed to detect gravitational waves. The rest of the projects, says the report, will have to wait their turn.

Making a queue for these missions is critical given the limited funding for new science initiatives at NASA. The NRC panel, led by Charles Kennel, an atmospheric scientist and physicist at the University of California, San Diego, also broke new ground by developing independent cost estimates for missions that are not yet in NASA's pipeline—and by concluding that each project team had seriously underestimated the cost of building and operating the spacecraft. It said Constellation-X, an advanced x-ray telescope, for example, would cost $3 billion rather than $2.1 billion. And with a program budget expected to rise from only $37 million in 2009 to $211 million in 2012, Beyond Einstein seems incapable of supporting more than one mission in the near future. "Our task was to address a mission which could fit [into a] budget wedge opening up in 2009," Kennel explained to reporters.

JDEM's success was due to both its scientific appeal and the maturity of its technology, panel members said. DOE's promise of up to $400 million didn't hurt. Saul Perlmutter, a DOE Lawrence Berkeley National Laboratory physicist and co–principal investigator on one of the three different proposed versions of the project, says that JDEM could be launched by 2015 and that the project has benefited from $40 million from DOE during the past 3 years. LISA, estimated to cost $2.75 billion rather than $2 billion, is another project counting on outside funding, with the European Space Agency (ESA) offering to foot $600 million of the bill. Kennel says the panel found LISA "an enchanting and technologically exciting mission" but suggested that NASA make no further plans until after the Pathfinder spacecraft, an ESA/NASA mission that will test LISA technologies, flies in late 2009. "We felt that in the long term, LISA will be the Beyond Einstein flagship," Kennel noted. "But it will not be ready in 2009."

In contrast, the NRC panel recommended kicking Constellation-X out of the Beyond Einstein tent because its contributions to science are likely to extend beyond the scope of the initiative. "Beyond Einstein is not the sole justification [for Constellation-X] or its primary benefit to the science community," the report concludes. Another mark against it is a price tag that is comparable to one of NASA's major observatories, and $900 million above the previous projection.

Bringing up the rear are the Black Hole Finder Probe and Inflation Probe, a ranking that didn't surprise backers of those two projects. "The competition was intense," says Harvard University astrophysicist Jonathan Grindlay, principal investigator on one of the two black-hole projects. The committee found a number of problems with the probe, which is

SOURCE: NATIONAL RESEARCH COUNCIL

Resetting the circadian clock
1488

Dengue vaccine challenges
1494

designed to find black holes of all sizes, including the difficulty in pinpointing low-luminosity black holes, questions about whether it could accurately determine growth rate of black holes, and uncertainty in identifying the galaxies in which they reside. It also gave a cost that's roughly double the initial $1 billion estimate. Grindlay disputes the new price tag, which he calls "way out of line," and adds that the committee ignored recent findings on high-redshift gamma-ray bursts that are beacons for black-hole creation.

Other researchers give the NRC panel high marks for weighing the science that could be done before considering schedules and cost. "There were so many good ideas, they had a tough choice," says Bradley Schaefer, an astrophysicist at Louisiana State University in Baton Rouge. NASA officials were also pleased with the results. "We're happy with what they've accomplished," says Jon Morse, NASA astrophysics chief, emphasizing the importance of a fiscally realistic plan. "We need to contain irrational exuberance."

–ANDREW LAWLER

U.S. NATIONAL SECURITY

Scientists Fear Curbs on Access to Satellite Data

For more than 3 decades, U.S. science agencies have used images taken by the nation's spy satellites to study everything from erupting volcanoes to the migration of marine mammals. Now, a new plan to expand the use of the satellites for homeland security and law enforcement has left some officials worried that science will suffer.

Last month's announcement by the Department of Homeland Security (DHS) that it was setting up a new National Applications Office (NAO) this fall to widen the use of spy-satellite imagery has sparked protests from civil liberties advocates. They worry that federal, state, and local authorities will seek high-resolution, real-time images to monitor activities of U.S. citizens in the same way that the satellites help track terrorist activities overseas. But officials at federal science agencies are concerned for a different reason: They suspect that the new arrangement could mean fewer chances to investigate scientific questions or cause delays that undermine the value of the information.

The satellites are operated by defense agencies and used mainly for reconnaissance overseas. Federal scientists can ask for permission to see specific images—as well as request that specific images to be taken—by applying to the Civil Applications Committee (CAC). Recommendations from the committee, which is headed by the director of the U.S. Geological Survey (USGS) and includes officials from more than a dozen agencies, are reviewed by the National Geospatial-Intelligence Agency (NGA), which oversees military and intelligence mapping efforts. Last year, CAC forwarded about 50 such requests.

Researchers have used the program to access images of phenomena such as the movement of glaciers in Yakutat Bay in Alaska, forest fires in Montana, and Mount Pinatubo in the Philippines. "If we are concerned that a volcano is about to erupt, we would like to be able to get the data now," says James Devine, an adviser to USGS director and CAC chair Mark Myers.

The big picture. Spy-satellite images have helped scientists study forest fires and other phenomena.

Under the new plan, CAC will report to NAO in parallel with two new working groups that will serve homeland security and law enforcement. NAO will take requests from all three working groups and pass them on to NGA, essentially adding a layer of bureaucracy. Some CAC members fear that scientific requests will end up at the bottom of the queue, far behind requests such as aerial images of vehicles at the U.S.–Mexico border. Science officials are also concerned that disagreements over privacy could lead Congress to decide that only intelligence agencies can use the data.

Some legislators have expressed similar apprehensions. In a 16 August letter to DHS Secretary Michael Chertoff, Representative Edward Markey (D–MA) asked the agency to describe how it plans "to ensure that vital scientific activities are not eroded" as the program expands "to include homeland security objectives."

DHS officials say those fears are unfounded. Speaking to *Science* at a House hearing last week on the new office, Charles Allen, DHS chief intelligence officer, said that the scientific program "is going to become more robust than ever. We are going to work hard for all of our customers, including science agencies."

CAC members say they won't know if science is being served until they learn more about the new office. "The people in charge have been a group of scientists representing their respective agencies," says another CAC member who requested anonymity. "With the program moving toward some sort of a domestic surveillance mission, can the science continue as before? I don't know."

–YUDHIJIT BHATTACHARJEE

CREDIT: GETTY IMAGES

Extra enzymes. Hadza diet drives gene copying.

CREDIT: F. MARLOWE/FLORIDA STATE UNIVERSITY

GENOMICS

A Little Gene Xeroxing Goes a Long Way

Researchers studying the evolution of starch digestion have uncovered evidence of a surprising adaptation: Rather than relying on mutations in a particular gene to help us digest roots and tubers better, the human genome simply made more copies of the gene in question. The finding is one of the strongest examples yet of evolution affecting gene copy number in humans and sheds light on how our diet split us apart from other primates.

An enzyme called salivary amylase—encoded by the *AMY1* gene—helps humans digest starchy food. In a typical evolutionary scenario, natural selection would favor random mutations in *AMY1* that caused it to churn out more of the enzyme or a more effective version of it in people who ate a high-starch diet.

But a study published online 9 September in *Nature Genetics* contends that something else happened. Nathaniel Dominy, an evolutionary anthropologist at the University of California, Santa Cruz, and George Perry at Arizona State University in Tempe analyzed *AMY1* in high-starch eaters such as Americans of European descent, Japanese, and Hadza from Tanzania, hunter-gatherers who eat many roots and tubers, as well as groups that eat little starch, such as the Biaka of the Central African Republic and the Mbuti from Congo, both rainforest hunter-gatherers, and Tanzania's Datog and Siberia's Yakut pastoralists. In all, the researchers studied samples from more than 200 people.

The team found that rather than having mutations that boosted *AMY1*'s activity, the high-starch eaters had extra copies of the gene. On average, the high-starch eaters had seven copies of the gene, whereas the low-starch populations had only five. "If you have a gene that's working well, why not just copy it over and over again?" asks Dominy. "Why wait for evolution to just roll the dice?"

For a broader evolutionary perspective, the researchers looked at 15 chimpanzees, which eat little starch. All had only two copies of *AMY1*. And an analysis of the gene from bonobos, the chimp's closest relative, found that it had mutations that may prevent *AMY1* from functioning altogether. "I was very excited to see this," says Gregory Laden, a biological anthropologist at the University of Minnesota, Twin Cities, who contends that eating starch-rich roots and tubers played a key role in differentiating humans from other apes.

Ajit Varki, who studies human origins at the University of California, San Diego, says the report also suggests that humans may have had access to starchy foods before the advent of agriculture, as is commonly thought. Even populations with low-starch diets had extra *AMY1* copies, he notes: "This would imply that first there were some rounds of duplication of the gene in preagricultural humans, and then that went further in agricultural humans."

–JON COHEN

Still Waiting for Cybrids

Despite a provisional okay from British regulators, scientists who want to use animal eggs as part of a process to produce patient-specific embryonic stem (ES) cells will have to wait a bit longer for the expected green light. Two U.K. groups have applied to that country's Human Fertilisation and Embryology Authority (HFEA) to try nuclear transfer techniques that would combine human cell nuclei and animal oocytes to create so-called cybrids. The technique, which U.S. and Chinese scientists have tried with limited success, might allow researchers to make patient-specific ES cells without using human oocytes, which are difficult to obtain.

After a yearlong review, HFEA said last week that it saw no fundamental reason to prohibit the technique but that it plans to make a decision in November after additional study. Stephen Minger of King's College London, who submitted his application in November 2006, says he is satisfied with the British regulatory process. "I like the fact that this [research] is tightly regulated. I think we've come out the other end with a huge amount of support" from the public.

–GRETCHEN VOGEL

Stem Cell Funding Plans

German scientists hoping for a relaxation of the strict laws governing human embryonic stem (ES) cells won't be getting any help from education and research minister Annette Schavan. This fall, the German parliament is expected to debate the country's current stem cell regulations, which make it a crime to work with human ES cells derived after 1 January 2002. This week, Schavan said she would not support lifting the cutoff date, although she did not rule out shifting it to allow work with more recently derived cells. At the same time, Schavan announced $6.85 million in new funding for research into methods that would produce pluripotent cells—cells that can become nearly all the body's cell types—without using human embryos. She says her goal is to make ES cells "superfluous."

As Germany continues to tread cautiously, California is speeding toward its goal of becoming the world's stem cell mecca. On 10 September, the Eli and Edythe L. Broad Foundation announced a $20 million donation to the University of California, Los Angeles, for faculty development, equipment, and facilities at its stem cell institute, now renamed after the donors. Last year, the foundation gave $25 million to the University of Southern California in Los Angeles for the same purpose.

–GRETCHEN VOGEL AND CONSTANCE HOLDEN

CONSERVATION

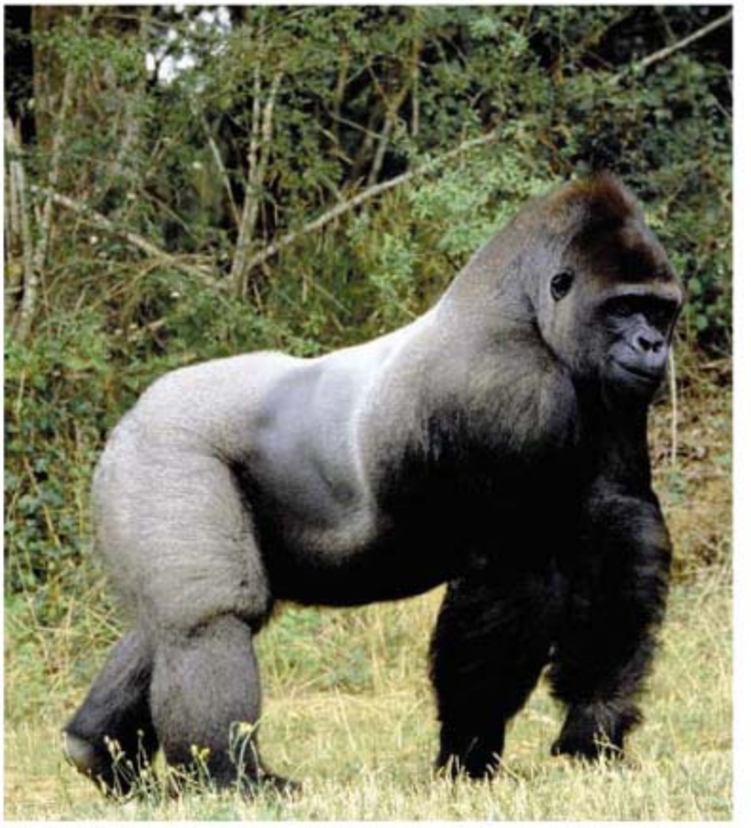
Scientists Say Ebola Has Pushed Western Gorillas to the Brink

The combined threat of the Ebola virus and poaching have pushed western gorillas into the "critically endangered" category in the latest international ranking of species threatened with extinction. Although estimates suggest that tens of thousands of the animals still live in west-central Africa, the new Red List from the World Conservation Union (IUCN) moves the species into its highest alert category, in large part because of fears that continuing Ebola outbreaks could swiftly wipe out still-significant gorilla populations.

The list, released on 12 September, highlights the western gorilla as well as dozens of other species for which new data indicate an increased risk of extinction. The "critically endangered" category is usually applied when just a few hundred individuals survive in the wild. But researchers say that western gorillas, despite their relatively large numbers, are in serious trouble. An ongoing series of Ebola outbreaks has killed up to 90% of the animals in some regions (*Science*, 8 December 2006, p. 1522), and the use of vaccines to stem the disease faces daunting challenges. Adding to the pressure, the rapid development of logging roads has opened up vast new regions to poaching and the bush-meat trade.

Although the other species in the *Gorilla* genus, the eastern gorilla, is far less numerous than the western gorilla, IUCN ranks the former one level lower at "endangered" because it is outside the current area of Ebola outbreaks. As for western gorillas, there may be as many as 30,000 left in their current range, which stretches across Gabon, Equatorial Guinea, and parts of Cameroon, the Central African Republic, and the Republic of the Congo. There are two subspecies, the more common western lowland gorilla and the extremely rare Cross River gorilla, of which fewer than 200 probably remain.

It is unusual for disease to be cited as a reason for reclassification, says wildlife disease specialist Richard Kock of the Zoological Society of London, who co-chairs the IUCN Veterinary Specialist Group. But even if the new status has come sooner than expected, the change is warranted, says Kenneth Cameron, a field veterinarian with the Wildlife Conservation Society in Brazzaville, Republic of the Congo. "Is this jumping the gun a bit? Some would argue that it is," he says. "But it is inevitable that this species is going to end up on a critically endangered list. It's simply a matter of when."



At risk. The threat from the deadly Ebola virus and poaching have prompted scientists to call western gorillas critically endangered.

IUCN experts found that the western gorilla population has declined by 60% in the past 20 to 25 years and estimated that in the past 15 years Ebola has killed one-third of the animals living in protected areas such as national parks. Those numbers are only the roughest of estimates, Kock says. The current gorilla range "is a huge place. … It's bloody impossible to know what's going on" in the remote forest regions, he says.

Conservationists say they hope the new status will help pressure governments and international donors to increase efforts to protect gorillas and their habitat. They also say they hope it will lead to more funding for the search for an Ebola vaccine.

What is certain is that western gorilla habitat will be under severe pressure in the next 5 years, Cameron says. Plans are under way in the Republic of the Congo to improve the road and rail connections between Brazzaville and Ouesso, the largest town in the north. Both projects will cut through prime gorilla habitat, making it easier for hunters to reach and for bush meat to be shipped back to city markets.

While public awareness campaigns and increased antipoaching efforts might help mitigate pressure from hunters, scientists are struggling to blunt the impact of Ebola. The virus can pass from ape to ape, so regions with higher population densities are especially at risk. "It appears to act like a brushfire," Cameron says. "You get a lightning strike somewhere, and it starts to burn."

Although admitting it's a long shot, some researchers hope a vaccine campaign could at least save enough animals to preserve the species. At least half a dozen vaccine candidates have protected mice or monkeys in the lab from the Ebola virus. But finding a way to deliver a vaccine safely to wild animals is no small challenge.

Few believe that vaccine-laden darts could reach enough gorillas to stem the spread of the disease. Peter Walsh of the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, is working with a vaccine company to develop possible baits that could carry an oral vaccine. The bait must keep the vaccine viable in the hot, humid conditions of the forest, attract great apes, and be safe for other animals who might find it first. Walsh says that before the end of the year, he and his colleagues plan to begin testing darting and oral bait strategies, without incorporating a vaccine, in the Republic of the Congo.

"This is not just about Ebola," Walsh says. "All apes are under increased disease threat, especially from human-introduced diseases. Vaccines are going to be an increasing part of conservation. … This is not going to be wasted time or money."

–GRETCHEN VOGEL

CREDIT: M. WATSON/WWW.ARDEA.COM

EPIDEMIOLOGY

Tropical Disease Follows Mosquitoes to Europe

For years, medical entomologists have worried that the astonishing ascent of the Asian tiger mosquito (*Aedes albopictus*) might bring not only nasty bites but also new public health surprises. After all, the mosquito is a known vector for more than 20 viral diseases.

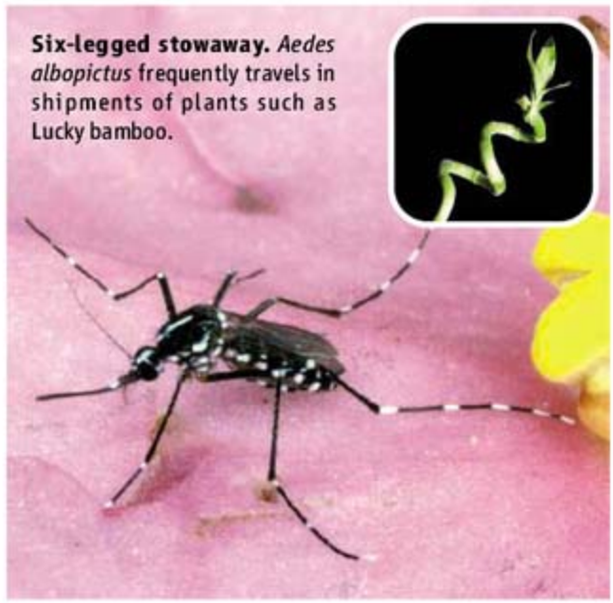
They were right. This summer, the mosquito, which has become firmly established in southern Europe, has infected almost 200 people in Italy with chikungunya, a painful viral disease. It's the first known example of chikungunya transmission outside the tropics—and it's making scientists wonder whether *A. albopictus* has the potential to touch off much larger outbreaks in Europe and the United States.

Chikungunya is rarely fatal but can cause severe fevers, headaches, fatigue, nausea, and muscle and joint pains. People started falling ill in Castiglione di Cervia and Castiglione di Ravenna—two villages separated by a river in the province of Ravenna—in early July, says Antonio Cassone of the Istituto Superiore di Sanità (ISS), a national government lab in Rome. But most patients' symptoms were mild and resembled those of other diseases, such as the Toscana virus, so health officials didn't notice for a while. Samples reached ISS on 27 August, and the virus was identified the next day.

Epidemiological detective work suggests that the index patient was a man who traveled to one of the villages and became sick there, after having been infected in India. Isolation and sequencing of the virus are under way to confirm that theory, Cassone says. One patient, an 83-year-old man with severe preexisting medical problems, has died.

Chikungunya sickened more than one-third of the almost 800,000 inhabitants of La Réunion, a French island in the Indian Ocean, in 2005 and 2006 (*Science*, 24 February 2006, p. 1085). India suffered an explosive outbreak in 2006 with more than 1.25 million cases, although some believe the real toll is much higher. Several European countries had seen "imported" cases of chikungunya lately, but local transmission in Europe has never been observed before. "It's fascinating," says entomologist Paul Reiter of the Pasteur Institute in Paris.

A daytime biter, *A. albopictus* originated in Southeast Asia and has made impressive strides across the globe in the past 2 decades. It was first found in the United States in secondhand tires imported from Asia in Houston, Texas, in 1985; today, it has spread to more than 20 southern and eastern states. In Europe, the mosquito has appeared in Mediterranean countries from Greece to Spain and as far north as the Netherlands. Its eggs often hitch a ride with plants shipped in water containers, such as the popular Lucky bamboo.



Six-legged stowaway. *Aedes albopictus* frequently travels in shipments of plants such as Lucky bamboo.

It's too early to tell whether chikungunya now has a permanent foothold in Europe. New cases have slowed to a trickle, says Cassone, in part because the mosquito population is dwindling as temperatures drop. A critical question is whether infected mosquitoes can survive the winter or pass on the virus to their offspring via their eggs, says Reiter. "If they can, we might see a rip-roaring epidemic next year," he says. Even if they can't, any newly imported case could kick off an outbreak in the future.

There are no drugs or vaccines against chikungunya, but the outbreak at La Réunion triggered renewed interest in an old vaccine candidate developed in the 1980s by a U.S. Army lab in Fort Detrick, Maryland. Scientists at three French government institutions are now working on that vaccine, and new clinical trials might begin before the end of 2008, says epidemiologist Antoine Flahault, who chaired a French task force on chikungunya last year.

–MARTIN ENSERINK

CREDITS (TOP TO BOTTOM): TIM ROBERTS/GETTY IMAGES; GETTY IMAGES

The Full Taleyarkhan

It looks as though bubble fusion researcher Rusi Taleyarkhan of Purdue University in West Lafayette, Indiana, will go under the microscope after all. Last week, Purdue officials announced that an internal panel has concluded that allegations of research misconduct warrant a full investigation.

The latest inquiry was prompted by a request from the Office of Naval Research (ONR), which helped fund some of Taleyarkhan's work, and follows congressional criticism of Purdue's handling of the alleged misconduct. The decision reverses a previous inquiry by the university that recommended against a full investigation (*Science*, 16 February, p. 921). Purdue expects to begin the investigation once it hears back from ONR officials.

–ROBERT F. SERVICE

Show Me the Data

Many gene hunters who trawl the entire human genome for disease genes will soon be asked to share their data. Starting 25 January, recipients of grants from the National Institutes of Health (NIH) for "genomewide association studies" will be "strongly encouraged" to submit their data sets stripped of identifiers to a central database. The sharing will allow findings to be validated in many populations (*Science*, 11 May, p. 820).

NIH will give researchers who submit data sets a year to publish before others can use the data in their own publications. Privacy protections would prevent nonresearchers from using the Freedom of Information Act to obtain genetic and clinical data on an individual, NIH concluded. One academic says she hopes NIH will spell out how institutional review boards should comply with the policy.

–JOCELYN KAISER

Florida Bound?

Germany's Max Planck Institute (MPI) is a big step closer to opening its first research center in the United States. This week, county commissioners in Palm Beach, Florida, unanimously supported the idea of selling $86.9 million in bonds as part of a $181.8 million incentive package to lure the institute. If the state kicks in its share, MPI will build a 9000-m^2 bioimaging research facility on the campus of Florida Atlantic University in Jupiter, next door to newly arrived Scripps Florida. "I've spent about 10 seconds considering this," says Commissioner Jeff Koons. "[Then] I said, 'Go do it.'" MPI officials called the vote "an important steppingstone."

–ROBERT F. SERVICE

BIOSECURITY

Reports Blame Animal Health Lab In Foot-and-Mouth Whodunit

Neglected, leaky pipes and England's record-setting wet summer likely combined to cause the country's recent outbreak of foot-and-mouth disease (FMD), according to two reports issued last week. The virus responsible probably escaped from a company, Merial, that grew vast amounts of it for vaccine production, the studies say. Yet the reports assign most of the blame for the outbreak to the Institute for Animal Health (IAH), a government lab at the same site in Pirbright that owned the aging network of underground wastewater pipes and was aware that it needed maintenance. IAH breached biosecurity in other ways as well, the reports found.

The findings are a blow to the reputation of IAH, a world-renowned FMD research center, says Andrew Mathieson, an environmental health expert at the University of the West of England in Bristol. But they should also serve as a more general warning. "My worry is: What about the many other research establishments of the same age?" he says.

Rapid government action helped contain the FMD outbreak, first confirmed on 3 August, to just two farms in Surrey (*Science*, 10 August, p. 732). Still, the National Farmers' Union puts the accident's economic impact at more than $100 million, and some politicians have called for resignations at the Department for Environment, Food and Rural Affairs (Defra), which oversees biosafety at IAH and also funds some 65% of its work.

Genomic comparisons of the outbreak virus to strains from Merial and IAH can't pinpoint from which of the two labs the virus escaped, according to the reports, one led by the U.K.'s Health and Safety Executive (HSE), a government agency, and the other by molecular epidemiologist Brian Spratt of Imperial College London. Still, the panels say, it's much more likely that the virus came from Merial, which grew it in two 6000-liter vats shortly before the accident, producing a million times more virus than IAH used in its small-scale experiments.

But how did it escape? The reports conclude that air leaks, contamination from solid waste, and foul play by terrorists or disgruntled employees are unlikely. Instead, both focus their suspicions on the site's wastewater system.

A two-step chemical strategy is used at Pirbright to prevent FMD from escaping in liquid waste. Both Merial and IAH first treat wastewater at their own buildings with a disinfectant such as citric acid. Then, a complex system of pipes takes the water to a shared effluent treatment plant, managed by IAH, where caustic soda is used to raise the pH to 12 and kill off any remaining virus during a 12-hour holding period. Finally, the liquid is released into the sewer.

Although the first treatment step probably killed off almost any leftover virus at IAH, it likely didn't inactivate the larger amounts in Merial's wastewater. The second treatment step would normally take care of that, but the network of pipes, pumps, and manholes leading to it suffered from leaks due to cracks, tree roots, and other problems. The reports hypothesize that live virus seeped into the soil as a result, especially because July's excessive rainfall may have caused the drains to overflow.

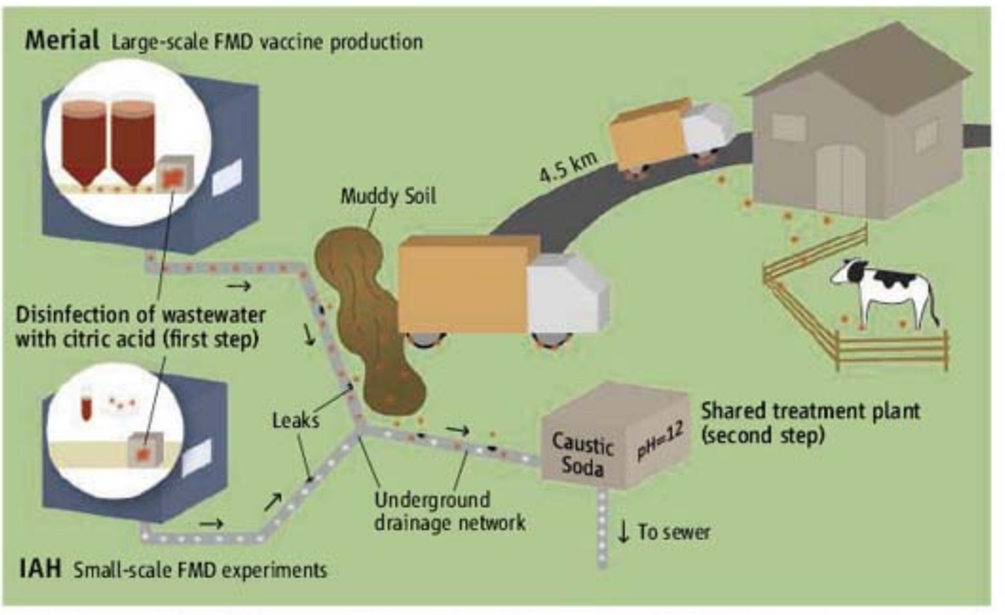
As it happened, construction crews were digging holes around the leaks at the time, and heavy trucks—without proper IAH oversight—drove through the presumably virus-laden mud. Some of these vehicles later took a road that went very close to the first infected farm. From there, the farmer may have carried the virus to his herd.

IAH, a part of the U.K. Biotechnology and Biological Sciences Research Council (BBSRC), owns the antiquated drainage system, the HSE report says. It was also aware of some of the network's problems. In fact, IAH, Defra, BBSRC, and Merial had debated an upgrade since 2003; the problem was money.

As to Merial's discharge of virus into its wastewater, HSE says this wasn't a breach of biosecurity, because Defra had approved the procedure used in the first disinfection step. But in a statement, IAH pointed its finger at Merial, suggesting that the company should have taken better care to inactivate any virus. Strangely, the Spratt report says, IAH didn't seem to know that Merial might release active virus into the system; biosafety officers from the lab and the company hardly ever talked.

Both panels question the wisdom of chemically inactivating wastewater altogether. Indeed, most modern labs use thermal inactivation—that is, pressure-cooking at 121°C—to destroy any pathogens, says Lee Thompson, a biosafety officer at the University of Texas Medical Branch in Galveston. Still, the second step, using caustic soda, "is very effective against FMD," Thompson says—but underground pipes that cannot be inspected "are a big problem."

Defra says it will adopt a range of recommendations to fix problems at Pirbright, such as keeping better track of visitors and making sure biosafety officers communicate. Merial has agreed not to grow live virus until U.K. authorities give it the green light. IAH, which was constructed in 1924, is due to be almost completely rebuilt by 2012, although some funding issues remain. Defra has also asked Health and Safety Commission chair Bill Callaghan to review the regulatory framework for animal pathogens. He is due to report by December. **–MARTIN ENSERINK**



Recipe for an outbreak. The escaped foot-and-mouth disease virus (red) probably originated at vaccine manufacturer Merial, two reports say, but the Institute for Animal Health owns the leaky drainage system that presumably let the virus seep into the soil. Trucks may have then carried it close to a farm.

SOURCE: J. NEWFIELD/SCIENCE

Under fire. Texas A&M University was faulted for lapses in its oversight of pathogen research.

BIODEFENSE RESEARCH

Lapses in Biosafety Spark Concern

An apparent breakdown in biosafety at Texas A&M University (TAMU) in College Station is prompting scrutiny of the expansive U.S. biodefense research program and the assurance that federal inspections keep researchers following the rules. Last week, the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, described a dozen safety lapses at TAMU, from unreported exposure to pathogens to inadequate protective gear. TAMU's research on select agents, pathogens that are considered potential bioweapons, is on hold until it complies with the regulations.

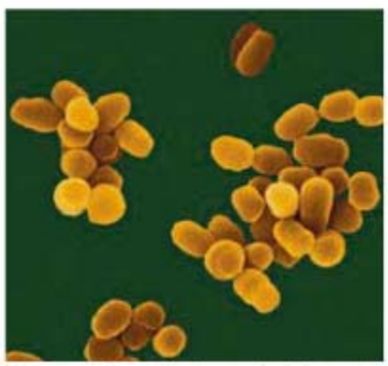
But in a twist, CDC may have indicted itself along with TAMU. Toward the end of a 21-page report, it noted that it had inspected TAMU as recently as February and found nothing other than minor problems, such as variation in how staff tracked lab inventory. After prodding by an independent whistleblower, however, CDC inspectors returned to TAMU in July and uncovered the violations described in last week's report, many from before the February inspection.

Biosafety and bioweapons experts say the charges are among the most damning that they can recall. They include three missing vials of *Brucella* bacteria; unauthorized employees working with select agents; a faculty member performing a recombinant DNA experiment without the necessary CDC approval; concerns about disposal of animals used in select-agent experiments; and three unreported cases of individuals exposed to the bacterium *Coxiella burnetii*, which causes Q fever, a treatable but infectious disease. "There was no evidence that a coordinated response or biosafety assessment was performed as a result" of these exposures, notes the CDC report.

The report "reflects about as badly on CDC as it does on Texas A&M," says Edward Hammond, director of the Sunshine Project in Austin, Texas, a bioweapons watchdog group. Last spring, Hammond's repeated demand for TAMU documents under a state open-records law revealed that in April 2006, an employee was diagnosed with brucellosis, an animal disease. TAMU did not report the infection to CDC until after it came to light (*Science*, 20 April, p. 353). Inspectors initially missed the "train wreck of a select-agent program," says Hammond. CDC has "got some explaining to do."

The agency declined to comment. "There's nothing I can add," said CDC spokesperson Von Roebuck, when asked whether the agency would speak to its failure to detect the major safety violations in its February inspection of TAMU.

One possible explanation, says Ronald Atlas, a microbiologist at the University of Louisville in Kentucky, is that normally, "the inspections are of the lab facility" and equipment, not an in-depth look at lab procedures. Many of the TAMU violations, however, concern access to pathogens and lab practices.



Exposed. *Brucella* bacteria infected a researcher, but the case went unreported for a year.

The problems CDC cited are serious but probably not unique, according to scientists both inside and outside TAMU. "If you were to apply an equivalent level of scrutiny at other institutions, I think you would find issues of concern," says TAMU microbiologist Vernon Tesh, one of four lab leaders singled out for safety lapses in CDC's report. "You always have to have safety in mind," he added. "Having said that, accidents happen." In a press conference last week, TAMU's interim president Eddie Davis said that other "institutions under that same level of review would probably have findings that would be reportable to the CDC."

Since the CDC's July inspection, the university's vice president of research and overseer of biosafety compliance, Richard Ewing, has resigned from his position and returned to the mathematics department (*Science*, 17 August, p. 879). Another biosafety official, Brent Mattox, also left his post. Davis declined to assign responsibility for the lapses or say whether any employees would face disciplinary action. He praised Ewing for having "been very loyal and competent."

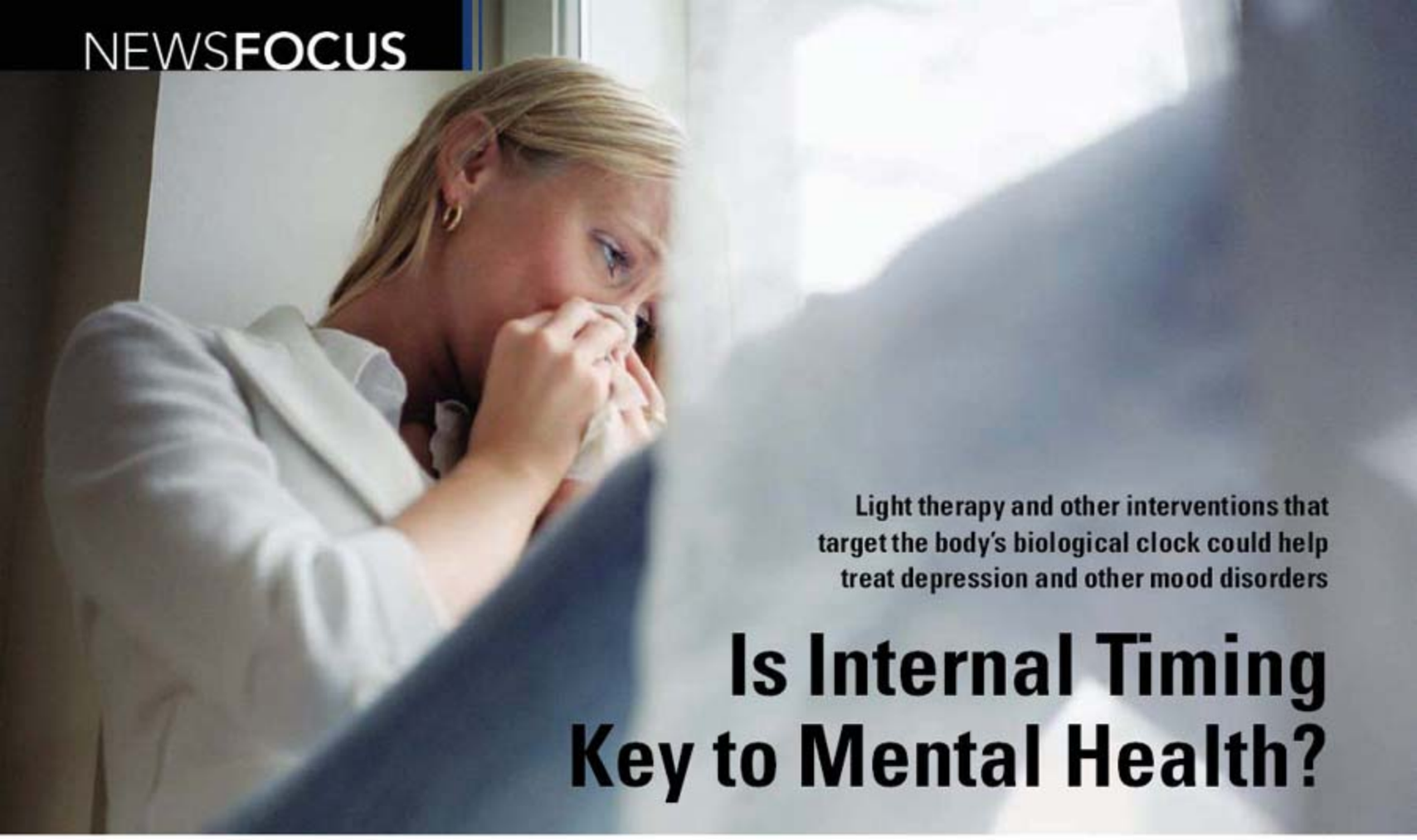
CDC has passed its report up the ranks to its parent agency, the Department of Health and Human Services, whose inspector general's office will consider whether to levy fines of up to $500,000 for each of the 12 violations. The Government Accountability Office, Congress's investigative arm, is looking beyond TAMU, examining risks associated with the growing number of high-level biosafety labs. The House Committee on Energy and Commerce plans to hold a hearing on the subject in early October.

Meanwhile, scientists wonder what effect the TAMU findings will have. "Biosafety is mandated by the public, or they're not going to let us do this research," says Atlas.

"This looks bad for all of us," says Philip Hauck, a biosafety professional in New York City. Abiding by the guidelines is essential, he says. But "people get blasé, I hate to say it. After a while as microbiologists, you're like, 'This thing never bit me.'"

–JENNIFER COUZIN

CREDITS (TOP TO BOTTOM): TEXAS A&M UNIVERSITY; DENNIS KUNKEL/VISUALS UNLIMITED



Light therapy and other interventions that target the body's biological clock could help treat depression and other mood disorders

Is Internal Timing Key to Mental Health?

EVERY YEAR, AFTER THE COLORS OF autumn faded from the trees and left barren branches to herald the winter, Herbert Kern would feel his mental skies darken. As the days shortened, the middle-aged materials researcher would retreat from almost all social interaction. The routine was so familiar to Kern's colleagues at Bell Labs in Murray Hill, New Jersey, that they would not expect much work from him during those winter months in the 1970s. The seasonality of Kern's depression was reflected in the pocket notebooks in which he kept a log of his life. "During the rest of the year, I could fill a notebook every 2 weeks; in the winter, it would take months," recalls Kern. Neither the few approved antidepressants of the time nor lithium injections did anything to help.

Then, in the late '70s, Kern learned about research in animals showing that melatonin, a hormone regulated by the light-dark cycle of day and night, plays a role in controlling seasonal behaviors such as mating. Wondering if the hormone had something to do with his condition, he got in touch with psychiatrist and melatonin specialist Alfred Lewy at the National Institute of Mental Health (NIMH) in Bethesda, Maryland, who was wrapping up a study demonstrating that exposure to bright light during the night suppressed nighttime secretion of the hormone in normal humans. When Kern sank into depression the following winter—in December 1980—Lewy's team exposed him to a few hours of light in the dark mornings and evenings, trying to match the amount of natural light of a spring day. After a few days of the treatment, "I began to be bubbly again," says Kern, who later continued the regimen at home. "It worked like magic."

Kern's case, and 3 years of follow-up work, led researchers to identify winter depression as a psychiatric illness that subsequently came to be known as seasonal affective disorder. SAD has since been shown to afflict millions of people, primarily in the northern latitudes, and a recent analysis by the American Psychiatric Association (APA) in Arlington, Virginia, provided a strong endorsement for light therapy as a treatment. And yet it's not settled how light, or other interventions that target the circadian clock, helps people with SAD.

SAD provides the strongest evidence to date of a link between the biological clock—the body's 24-hour timekeeper—and mental health, a proof of principle that circadian rhythms that are out of sync could underlie some mood disorders. But there is increasing evidence that circadian disturbances are involved in other common mental ailments such as bipolar disorder and more obscure ones such as a syndrome in which people compulsively eat at night. In recent years, psychiatrists working with small groups of patients have shown that correcting abnormal circadian rhythms—through exposure to light, melatonin pills, or even sleep deprivation—can help treat some of these disorders and can also benefit patients with neurodegenerative illnesses such as Alzheimer's. Some drug companies are even taking heed. "The circadian model is clearly beginning to bear fruit," says David Avery, a psychiatrist at the University of Washington School of Medicine in Seattle. "It is logically getting extended beyond SAD and should lead to better treatments for a number of psychiatric disorders."

The fog about light

When Kern contacted Lewy at NIMH, scientists already knew that all mammals have a master clock in the brain's suprachiasmatic nucleus, which regulates the waxing and waning concentration of numerous hormones and proteins in the body over an approximately 24-hour cycle. They also knew that the rhythms of many of these body chemicals—including melatonin, secreted by the pineal gland during darkness—were synchronized to the light-dark cycle of the environment. In treating Kern with light, the NIMH researchers—led by Lewy and his senior colleague, Thomas Wehr—simply simulated the earlier dawn and later dusk of

CREDIT: MIKA/ZEFA/CORBIS

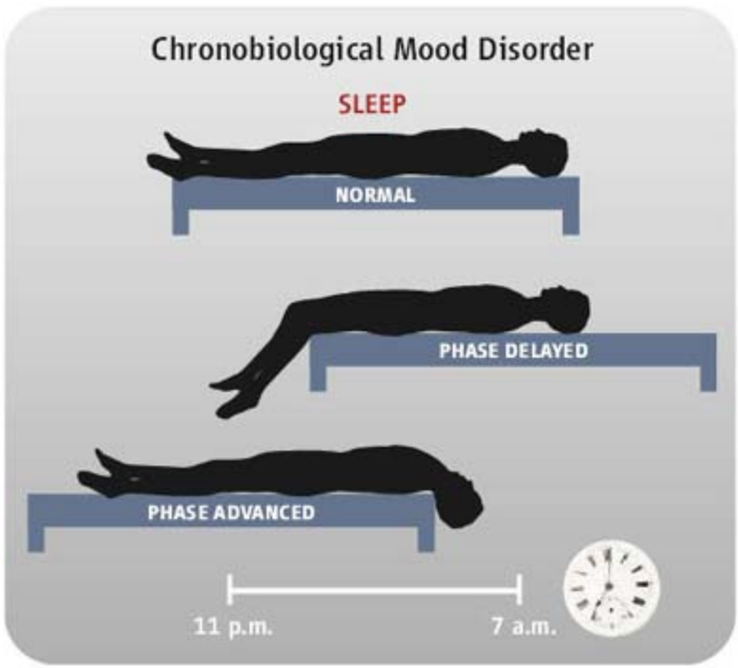
spring, hoping that by shortening the duration of melatonin secretion, they'd lift Kern out of his depression.

Although it worked—and has since proven effective in treating many other cases of SAD—Wehr and Lewy formed different opinions about light therapy's mechanism. Wehr grew convinced that the antidepressant effect was a result of the artificially lengthened daytime, which led to less melatonin secretion and presumably had downstream effects leading to an improvement in the patient's mood. Lewy instead came to believe that the effect was due to the resetting of the patient's circadian clock, not the overall duration of melatonin production. In most SAD patients, he argued, the depression was the result of circadian clocks being out of sync with respect to the sleep-wake cycle, like a chronic form of jet lag. The theory has become known as the phase-shift hypothesis.

Last year, researchers led by Lewy—who has been at Oregon Health and Science University in Portland since 1981—presented the strongest evidence to date for this theory. Rather than using bright lights to reset the circadian clock, Lewy and his colleagues gave SAD patients melatonin pills. (The body's melatonin rhythm is tightly coupled to rhythms of other hormones such as cortisol and serotonin, and researchers have established that administering melatonin is a way to shift all of those rhythms en bloc.) People normally start secreting melatonin a couple of hours before bedtime to prime the body for sleep, so administering the hormone in the afternoon should advance a patient's circadian clock relative to his sleep-wake cycle. If given in the morning, it should have the opposite effect.

By making patients stick to their regular sleep times, the researchers ensured that their sleep-wake cycle remained constant throughout the study. After 3 weeks, they found that SAD patients whose circadian clocks normally lagged behind their sleep-wake cycle did better when they received afternoon melatonin and worse when they were given the hormone in the morning. The treatments had the opposite effects on those whose cycles were shifted the other way. Lewy points out that the treatments increased the duration of melatonin production, yet patients improved when their cycles were brought into sync. "If Tom [Wehr] was right, these people should have gotten worse," he says. Lewy notes that the melatonin results are consistent with previous studies showing that morning light is significantly better at treating SAD than evening light (which corresponds to there being a higher proportion of phase-delayed rather than phase-advanced individuals among SAD patients).

Wehr, who retired from NIMH in 2003 and is now a practicing psychiatrist in Bethesda, Maryland, remains unconvinced. He points to animal studies showing that morning light brings about a quicker end to melatonin secretion without really affecting the hormone's onset time in the evening. It's possible, he argues, that afternoon melatonin led Lewy's patients to stop secreting the hormone a lot earlier than normal the following morning, in effect shortening the length of their melatonin production. To settle the question, Wehr says, researchers would need to keep a continuous track of the patients' 24-hour melatonin profile.



Out of sync. Some researchers believe that misalignments between certain circadian rhythms and the sleep-wake cycle may be a driver of mental illnesses.

SOURCE: A. LEWY/OHSU

Lewy's hypothesis does not rule out the possibility that additional mechanisms are involved in light's antidepressant action. Some studies have shown, for example, that exposure to sunlight can increase brain levels of serotonin—a neurotransmitter associated with well-being—and Lewy says it's possible that serotonin is related to circadian alignment. To get a full mechanistic account of the clock's role in mental health, researchers still need to understand what cellular events are triggered when out-of-sync rhythms are snapped back into phase with each other, and by the same token, what happens in the brain when rhythms go awry—as they do even in healthy individuals who are jet-lagged.

Beyond SAD

A better understanding of these mechanisms could shed light on disorders beyond SAD, for abnormal circadian rhythms are turning out to be a factor in a number of other mental illnesses. Two years ago, in *Chronobiology International*, Vishwajit Nimgaonkar and his colleagues at the University of Pittsburgh Medical Center in Pennsylvania reported that among 75 patients with bipolar disorder, internal biological clocks—as measured by a questionnaire probing activity and sleep patterns—tended to be disturbed in comparison to those of a set of normal individuals.

And in two ongoing studies, researchers led by Anna Wirz-Justice of the Centre for Chronobiology at the Psychiatric University Clinic in Basel, Switzerland, are finding abnormal circadian rhythms in schizophrenic patients and in patients with borderline personality disorder. (The preliminary results from the studies were presented at the annual meeting of the Society for Light Treatment and Biological Rhythms in Copenhagen, Denmark, in June.) Also this summer, at a meeting on biological clocks and rhythms at Cold Spring Harbor Laboratory in New York state, psychiatrist Namni Goel of the University of Pennsylvania reported that many 24-hour hormonal rhythms in patients with night eating syndrome were either advanced or delayed with respect to the sleep-wake cycle.

Some researchers suspect that defects in the gears of the body's biological clock, caused by genetic mutations, will be shown to play a role in mental health problems. They point to studies such as one reported last year by Colleen McClung and her colleagues at the University of Texas Southwestern Medical Center in Dallas. The researchers created mice missing the *Clock* gene—which encodes a key protein in the machinery of the circadian system—and found that the animals showed manic behaviors, becoming hyperactive and keener to take risks. Expressing the CLOCK protein in the animals' midbrains restored behavior of the mutant mice to normal, McClung and her colleagues further reported in the 10 April issue of the *Proceedings of the National Academy of Sciences this year*.

If disrupted circadian rhythms contribute to mental illnesses other than SAD, those conditions could also benefit from light therapy. Indeed, researchers have begun testing this idea in small groups of patients, and they say the results look promising.

Nearly 200 people with Alzheimer's disease, spread across 10 homes for the elderly, are now helping researchers test whether light therapy can alleviate some symptoms of the fatal neurodegenerative disease—one of which is disturbed sleep-wake rhythms. Psychiatrist Eus J. W. van Someren of the Netherlands Institute for Neuroscience in Amsterdam and his colleagues have installed bright light fixtures in the lounges of six of the homes; at the remaining sites, they installed similar but fewer lights to set up the lighting equivalent of a placebo. Van Someren says that the unpublished preliminary results, based on more than 4 years of data, show that bright light improved the sleep-wake rhythms of patients. He claims the data also show that it slowed their cognitive decline, hinting that the disturbed circadian rhythms were a partial cause.

Dispelling gloom. Psychiatrist Alfred Lewy wants to understand why light therapy (being set up, *above*) works in patients with seasonal affective disorder.

Light and melatonin are not the only interventions that researchers are using in their attempts to treat mental disorders by tinkering with the circadian clock. Francesco Benedetti, a psychiatrist at the San Raffaele Scientific Institute in Milan, Italy, has spent the last decade studying the antidepressant effects of total sleep deprivation—a strategy discovered by chance in the 1960s when German clinicians observed significant improvement in a depressed patient who had spent the night biking. Although how the technique works is poorly understood, psychiatrists routinely use sleep deprivation to produce a rapid emotional lift in deeply depressed patients, including those hospitalized after a failed suicide attempt.

Benedetti and others have shown that this dramatic effect, which invariably vanishes after a day, can be sustained for several weeks by using light therapy to shift the patient's sleep-wake cycle in the days that follow. The idea again is to bring the circadian rhythms back in alignment. The researchers have reported, in a study published in *The Journal of Clinical Psychiatry* in 2005, that combining light therapy with initial sleep deprivation can effectively treat bipolar patients. In a more recent study involving 55 bipolar patients, presented at the Cold Spring Harbor meeting by University of California, Irvine, psychiatrist Joseph Wu, those who received a treatment package including antidepressant medication, light therapy, and sleep-wake adjustment following total sleep deprivation did significantly better than those who only received medication.

Witch healers?

Such studies seem to be making an impression on the broader psychiatric community. In 2005, a group set up by APA to examine the efficacy of light therapy concluded from a meta-analysis of published literature that the treatment significantly reduced depression symptoms in SAD, as well as in other mood disorders. The group, led by psychiatrist Robert Golden, now at the University of Wisconsin School of Medicine and Public Health in Madison, declared in April 2005 in *The American Journal of Psychiatry* that "the effects of light therapy are comparable to those found in many antidepressant pharmacotherapy trials." However, the authors lamented the relatively small number of studies that met their criteria for the analysis—only 20 out of a total of 173 that were initially identified—and they noted that "additional randomized, controlled trials with appropriate numbers of subjects are needed."

Until even a few years ago, "people looked at us as if we were some kind of strange witch healers," says Benedetti, who began combining light therapy with sleep deprivation in the 1980s. Still, with recent data showing that drugs do not significantly help up to 40% of patients with mood disorders, he says, "there is a growing interest in chronobiological methods of treatment."

Unfortunately, proponents of such methods say, funding has been hard to come by, in part because of the perception that effective antidepressants are available. Michael Terman, a psychiatrist at Columbia University, recalls that one grant application turned down by the National Institutes of Health contained this comment: "Why do we need a new antidepressant modality when we already know that drugs work?" The proposed work, a randomized trial testing light therapy in pregnant women with depression, is now being funded by the Swiss National Science Foundation.

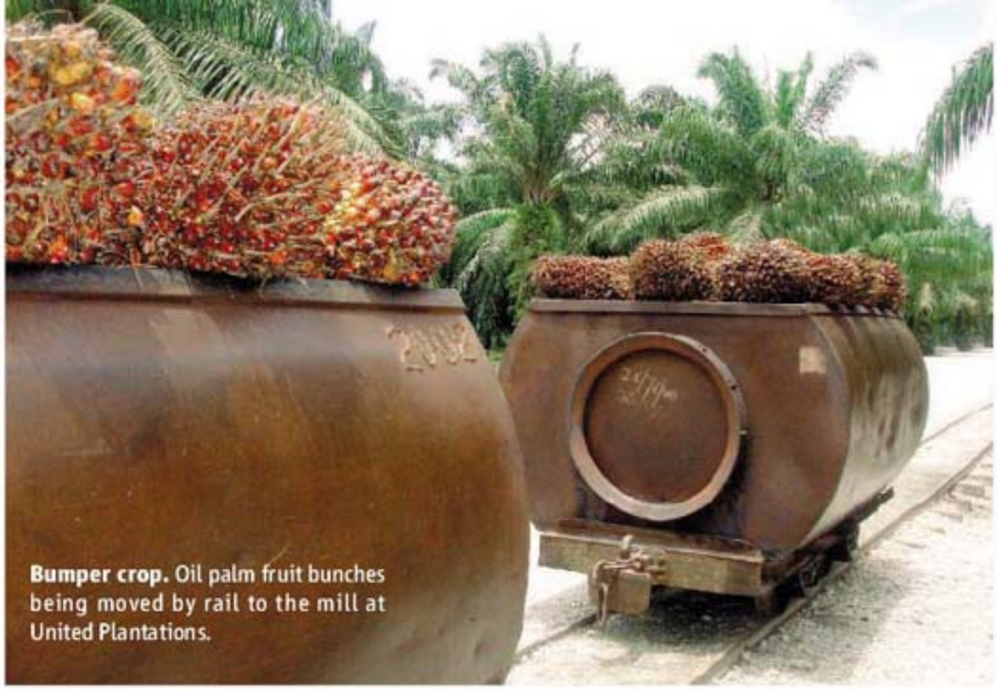
"The pharma-driven model is so strong that it is difficult to win support for studying anything that does not involve drugs," says Wirz-Justice.

Nonetheless, the French pharma company Servier has patented a melatonin agonist called agomelatine that is now undergoing clinical trials in Europe and in the United States as a treatment for depression. Merck has also set up a research group to look into the circadian basis of mood and sleep disorders in hopes of developing more effective drugs. "As therapies go, it would be far easier to pop a pill than carry around a fluorescent bulb," says Anthony Gotter, a member of the group.

Kern, who is now practically blind from macular degeneration, would welcome a pill substitute. He says that light therapy became less and less effective for him over the years as his eyesight faded. "Now I can hardly see, and all hell has broken loose," he says with surprising cheer in his voice. "I have had periods of depression lasting over a year, and highs lasting as long. I think my clock is just running freely, without any control by the environment. I don't know when I'm going to feel what."

–YUDHIJIT BHATTACHARJEE

CREDIT: R. D. YORK/OHSU MEDICAL PHOTOGRAPHY (PROVIDED BY A. LEWY/OHSU)



Bumper crop. Oil palm fruit bunches being moved by rail to the mill at United Plantations.

CREDIT: R. STONE/SCIENCE

ECOLOGY

Can Palm Oil Plantations Come Clean?

Under fire for their poor environmental record, makers of the world's top vegetable oil are turning to scientists for advice on how to make their industry sustainable

TELUK INTAN, MALAYSIA—A canary-yellow machine lumbers onto a fallow oil palm field and, with a roar of its motor, rips into a pile of fronds and shavings of dead trunks. As plantation operators and scientists observe the mulching process, their guide, Cheriachangel Mathews, a senior manager at United Plantations' Jendarata Estate, warns that the group has been infiltrated. "We have a journalist with us," he says. "I want him and all of you to know that nothing here—nothing—is wasted."

Mathews has good reason to be concerned about the take-home message. With prices soaring, palm oil, Malaysia's number-one crop, has recently surpassed soybean as the top-selling vegetable oil in the world. Oil squeezed from palm fruit bunches is an ingredient in myriad products, from ice cream to soap, and it is being touted as a biofuel that can stem reliance on fossil fuels. But the industry has been taking a mulching in the press. Environmental groups have accused plantations of razing forests to plant the lucrative crop and slaughtering orangutans that pilfer and eat the fruit.

Hoping to turn over a new frond, the oil palm industry is now endeavoring to demonstrate its sustainability. It faces an uphill battle. A just-completed review by three dozen academics details species declines pinned on the oil palm, a native of West Africa that has become a dominant feature of Southeast Asia's landscape. It is an "unavoidable fact that the replacement of diverse tropical forest with an exotic monoculture significantly impacts biodiversity," states the *Biodiversity and Oil Palm Briefing Document*. It will be presented at a gathering in November of the Roundtable on Sustainable Palm Oil (RSPO), in which industry officials, scientists, and other parties are hammering out a voluntary certification scheme for minimizing harm to the environment.

Scientists and like-minded industry insiders hoping to curb destructive growth may get help from the market. Rising palm oil prices are strangling demand for palm as a biofuel, Edgare Kerkwijk, managing director of the BioX Group, a renewable-energy company in Singapore, told the International Palm Oil Congress in Kuala Lumpur late last month. That's bitter news for companies in Southeast Asia that have been racing to ramp up capacity to process palm into biodiesel. With crude palm oil now topping $700 per ton, "we believe that palm oil is not a long-term biofuel," Kerkwijk said.

The industry, nevertheless, is riding high. According to the Food and Agriculture Organization of the United Nations (FAO), global palm oil production last year was 37 million tons, 85% from Indonesia and Malaysia. Palm oil yields—2.8 tons per hectare, on average—are seven times those of soybean oil, according to FAO. Aiming for even higher yields, the Asiatic Centre for Genome Technology in Kuala Lumpur and Synthetic Genomics, a company in Rockville, Maryland, founded by J. Craig Venter, in July announced a partnership to sequence and analyze the oil palm genome.

Higher yields are vital to an industry looking to clean up its act. Seen from the air, peninsular Malaysia is a patchwork of settlements and plantations interspersed with forest; in 2003, the peninsula had more than half of the country's 3.7 million hectares of oil palm. Malaysian officials maintain that plantations are now allowed to expand only onto existing agricultural fields or degraded land. Indonesia is a different story. There, renegade plantations fuel expansion through timber sales. "At the state level, there are no clear limits on plantation growth," says Reza Azmi, director of Wild Asia, a company in Kuala Lumpur that is advising plantations in both countries on how to limit their environmental footprint.

RSPO was formed 5 years ago to turn the positive environmental record of outfits such as United Plantations into a competitive advantage through the certification of "sustainable palm oil." To bolster this effort, a network of researchers drew on a wealth of data to assess the impact of plantations on biodiversity.

An advanced draft of the document provided to *Science* paints a grim picture. The authors, led by Emily Fitzherbert of the Zoological Society of London, summarize research documenting shifts in biodiversity in and around plantations. In Sumatra, for example, less than 10% of birds and mammals found in primary forests live in plantations, and more than 75% of bat species were lost; in Thailand, 41 bird species were found in plantations, compared to 108 species in nearby tropical forests. "Plantations need to accept that oil palm is not compatible with biodiversity," says report coauthor Matthew Struebig of Queen Mary, University of London, U.K. "Environmental groups and scientists need to work with, not against, the industry to help them minimize this impact."

The document delivers a clear bottom line to RSPO: "The most immediate and important action needed to prevent further biodiversity loss is to ensure that oil palm expansion does not contribute to deforestation." The report also highlights how proactive management can reduce species losses, for example by salvaging native stands inside plantations. Wild Asia is working with plantations on plans to link fragments into "natural corridors" and set aside 50 of every 2000 hectares for forest regeneration. "Two years ago," says Azmi, "this discussion would never have happened."

–RICHARD STONE

RESEARCH IN JAPAN

Big Winners, Big Expectations

Five groups have been awarded decade-long grants in a drive to win global attention and draw international talent

TOKYO—Immunologist Shizuo Akira is indisputably at the top of his field. For 2 years running, the Osaka University professor has been Thomson Scientific's "Hottest Researcher" for authoring the most highly cited papers in his field. But Osaka has not won recognition as a leading world center for immunology research; Akira fears the university may even be in danger of falling behind. Advancing technology "makes it very difficult for a single laboratory" to create an international buzz, he says: "What's needed is to accumulate a research team and get a big grant."

He has just gotten a very big grant; Japan hopes the international buzz will grow. Akira's center is one of five selected to receive in the neighborhood of $12 million per year for 10 years under a World Premier International Research Center Initiative sponsored by Japan's Ministry of Education. The grants, which must be supplemented by the host institutions, are intended to take the winners to a new level of global prominence through generous, discretionary funding and support for internationalizing research. Akira hopes to lure leading Japanese and foreign immunologists to Osaka and, in particular, push into the nascent field of in vivo imaging of the cell-cell interactions that define immune response.

The grant program is an audacious bet by Japan's Ministry of Finance, which is out to make at least this handful of centers as widely recognized as the Massachusetts Institute of Technology's Media Lab or the U.K.'s Laboratory of Molecular Biology in Cambridge. "It's a visionary program," says Matthew Mason, director of the Robotics Institute at Carnegie Mellon University in Pittsburgh, Pennsylvania. Mason was one of six foreign scientists on an international panel that reviewed 13 short-listed applications. The objective was to "pick groups already at the peak [of their field] and give them support to make them globally visible," says Hiroshi Ikukawa, who is heading development of the program for the Ministry of Education.

Tohoku University in Sendai, for example, proposed creating an atom-molecule-materials center around its Institute for Materials Research, which is already one of the world's most prolific material science groups. Yoshinori Yamamoto, slated to direct the new center, says they hope to take their work on bulk glass materials to a new level by adding theorists and computational scientists. The University of Tokyo is partly building on the breakthrough studies of neutrinos done at its Super-Kamiokande Neutrino Observatory with a new Institute for the Physics and Mathematics of the Universe. Hitoshi Murayama, a theoretical physicist at the University of California, Berkeley, says they will bring together experimental observations, theory, and new mathematical approaches "to try to understand such basic questions as how the universe started and where it's going."

Global visibility has eluded Japan's universities and research institutes for a variety of subtle reasons. Norio Nakatsuji, a cell biologist at Kyoto University who will be heading its new Institute for Integrated Cell-Material Sciences, cites geographical isolation and the language barrier. So the initiative has set a target for each center to have 10% to 20% of its two dozen or so principal investigators (PIs) and 30% of an expected 200 research staff be non-Japanese. And "naturally, English should be the language of the centers," says Nakatsuji.

Paul Weiss, a chemist at Pennsylvania State University in State College, who will be affiliated with the Tohoku center, says, "Another [problem] is the hierarchy typical in Japanese scientific institutions." To counter this, Weiss says, "we are making a concerted effort to encourage creativity and independence among young scientists."

And Masakazu Aono, director of the new Center for Materials Nanoarchitectonics at the National Institute for Materials Science in Tsukuba, says that probably because of rigid academic structures, "Japanese scientists have not been good at interdisciplinary collaboration." His center will bring a range of specialists together to study nanoscale structures to create new types of alloys and microelectronic devices as well as organic and biological materials.

Weiss, for one, is envious. "Where can we ask for resources in the U.S. to go after a 10-plus-year problem? What mechanism lets us put together a team of the top people from all over the world?" he asks.

Still, some researchers are concerned about the depth of commitment. "There is no tenure [in this program]," notes Murayama, who will head the new center at the University of Tokyo. "So how do we make the jobs at this institute competitive" with the best permanent jobs elsewhere? he asks. And there are questions about the involvement of the non-Japanese PIs. Most, including Weiss, will likely maintain their current positions, devoting just a percentage of their efforts to the centers.

Program backers hope the part-time presence of leading foreigners plus full-time Japanese scientists will attract younger researchers of all nationalities on a full-time basis. Kyoto's Nakatsuji says they have plans for "superpostdocs," under which select newly minted Ph.D.s could be given the money to independently run a small group, complete with technicians and graduate students. Osaka's Akira hopes some of these young scientists will become world leaders—and stay in Japan. **–DENNIS NORMILE**

CREDIT: (PHOTO) KAMIOKA OBSERVATORY, ICRR, THE UNIVERSITY OF TOKYO

Host Institution	New Institute Name	Objective
Kyoto University	Institute for Integrated Cell-Material Sciences	To understand and control chemical and physical processes at the cellular scale
Tohoku University	Research Center for Atom, Molecule, Materials	To promote the development of new materials, particularly bulk glass
University of Tokyo	Institute for the Physics and Mathematics of the Universe	To study basic questions about the origin, composition, and fate of the universe
Osaka University	Immunology Frontier Research Center	To merge imaging and immunology to study immune cell activity in vivo
National Institute for Materials Science	International Center for Materials Nanoarchitectonics	To study and control materials at the nano scale

New horizons. Findings at the Super-Kamiokande Neutrino Observatory at the University of Tokyo (*above*) led to a grant for an international math and physics institute.

TROPICAL DISEASES

Hunt for Dengue Vaccine Heats Up As the Disease Burden Grows

As the number of cases reaches an all-time high, new techniques and an influx of research funds could mean this long-neglected disease will finally have a vaccine

For decades, Duane Gubler and other arbovirus experts have been warning about a looming dengue crisis. But dengue fever, transmitted most often by the bite of an infected *Aedes aegypti* mosquito, was often seen as an obscure, only occasionally fatal disease of tropical countries, and progress toward a vaccine and drugs to treat it has been slow.

Now, with cases exploding across Southeast Asia and the disease apparently becoming more virulent and spreading into new geographic areas, vaccine research is taking on a new urgency. "For 30 years, we've been saying a dengue vaccine might be available in the next 10 years," says Gubler, a dengue expert at the University of Hawaii, Manoa, in Honolulu. "And now, finally, it seems we may be right about that." Some long-running research is finally bearing fruit, says Gubler, and as dengue captures global attention, the pharmaceutical industry is boosting investment in both traditional and novel vaccine technologies. The Bill and Melinda Gates Foundation in Seattle, Washington, has chipped in a $55 million, 5-year grant to set the stage for phase III trials, which will help speed candidate vaccines to market.

A vaccine can't come a moment too soon. On average, fewer than 300,000 cases of dengue a year were reported to the World Health Organization (WHO) during the 1980s; since 2000, that number has exploded to 925,000. Because surveillance is poor, WHO estimates that the true number of dengue cases tops 50 million annually, including about 400,000 cases of dengue hemorrhagic fever (DHF), a severe and sometimes fatal form of the disease. In Southeast Asia, dengue is starting to rival malaria as a killer of children, and its economic impact is already greater. The spike in cases is driven by the collision of several trends, chief among them rapid urbanization and to some extent poverty. The warm, crowded cities of Latin America and Asia provide an ideal habitat for the main vector, *A. aegypti*, which breeds in stagnant water and likes to feed on humans in quick succession. Faced with record-setting outbreaks this year in Southeast Asia, WHO sounded the alarm on 23 July, calling on countries to dramatically step up mosquito control—for now, the only means of prevention—and improve patient care. But to date, most developing country governments have a dismal record of mounting and sustaining effective vector-control programs. This means, Gubler says, "it's going to continue to get worse until we have a vaccine."

Rush hour. Periodic dengue outbreaks suddenly overwhelm hospitals with patients, such as these in a makeshift tent outside a military hopital in Indonesia.

CREDIT: DESI SARI/AP PHOTOS

A quadruple challenge

Dengue is caused by four closely related viral serotypes—dengue 1 through dengue 4—which are single-stranded RNA viruses spread primarily by the *A. aegypti* mosquito. The disease in humans ranges from mild to mortal. A week or so after infection, the typical patient suffers a rapid onset of fever with excruciating joint pain—dengue is called "breakbone fever" in some regions—and sometimes nausea and skin rashes. About 1% of cases progress to DHF, with internal bleeding that can lead to shock and death, although fluid replacement therapy usually saves those hospitalized in time.

Once they recover, patients are immune for life, but only to the dengue serotype that infected them. For poorly understood reasons, those subsequently infected with a second serotype are at far greater risk of progressing to DHF. Studies show that more than 90% of DHF patients had a previous dengue infection.

And the odds of DHF are increasing. The four serotypes used to be isolated geographically, making second infections rare. But, probably because of increased human mobility, now all four viruses often circulate in a region simultaneously. What's more, says John Ehrenberg, a WHO adviser on vector-borne diseases based in Manila, "the virus has changed genetically over the past 2 to 3 decades into more pathogenic strains." This makes first infections more serious and second infections even worse. "A lot more cases are ending up in hospital because of complications," Ehrenberg says.

A shot in the dark

Since work began in the 1940s, vaccine developers have tripped over one stumbling block after another. Early on, researchers feared that someone vaccinated against one type of dengue might suffer the immune-enhancement response leading to DHF if later infected with a different serotype. Avoiding this response requires a tetravalent vaccine that provides roughly equal and lasting protection to all four dengue serotypes. But decades of research have shown that "it is hard to make a tetravalent vaccine so [that] there is simultaneous immunity against all four [viruses]," says

Alan Barrett, a virologist at the University of Texas Medical Branch in Galveston. Ehrenberg adds that although other viruses also have different serotypes, only dengue provokes immune enhancement. Work has also been stymied by the difficulty of growing the virus in culture and by the lack of an animal model. Monkeys infected with dengue produce antibodies but don't really suffer from disease, limiting their experimental value.

Working separately, researchers at Mahidol University in Bangkok and at the Walter Reed Army Institute of Research (WRAIR) in Silver Spring, Maryland, were the first to report in the 1990s significant progress toward a tetravalent dengue vaccine. Both groups set their sights on a live attenuated vaccine, in which a live virus is weakened by repeated replication in a cell culture. Both groups struggled to find the right level of attenuation at which the virus is strong enough to trigger an immunogenic response but weakened enough so that it cannot cause illness. Without an animal model, the researchers had to develop techniques, such as how the virus affected different cell cultures, by which to judge attenuation. And they had to develop a different vaccine for each dengue serotype, test it in humans, combine them, and go through human trials again.

By the early 1990s, after more than a decade of development, the Mahidol group had combined attenuated strains of dengue 1, 2, and 4 into a vaccine that "got good results," says Sutee Yoksan, a virologist who heads Mahidol's Center for Vaccine Development. But when they added their dengue 3 vaccine to the cocktail, things went awry. Some volunteers got sick from the dengue 3 component, which also interfered with the production of antibodies, leaving those inoculated with little or no protection against the other three serotypes. The vaccine was licensed to what is now Sanofi Pasteur in Lyon, France, where researchers tried genetically weakening the dengue 3 component. But trials of this monovalent dengue 3 vaccine in 2002–2003 still sickened volunteers, and Sanofi Pasteur has given up on the vaccine. In Bangkok, Yoksan is still screening dengue 3 viruses for another attenuation candidate. "If we can solve the dengue 3 problem, we will have a good vaccine," he says—but he won't predict how long it might take.

The group at WRAIR also had trouble with its dengue 3 virus but eventually attenuated it. GlaxoSmithKline (GSK) has taken over clinical development of the vaccine and hopes to start a phase II field trial next year. Several thousand people in vaccinated and control groups will be tracked for 1 to 2 years to compare rates of infection.

Bruce Innis, a GSK physician and virologist who previously worked on the vaccine at WRAIR, says that except for a very limited trial in the early 1960s, this will be the first time a dengue vaccine will be tested for actually preventing illness, as opposed to simply measuring neutralizing antibody production. With most diseases, mice or monkeys can be challenged with infection to determine the efficacy of a candidate vaccine, but that doesn't work for dengue. In human trials so far, researchers have inferred the degree of efficacy by measuring the production of neutralizing antibodies in response to vaccination in human volunteers. "But we don't know how much antibody you need to have in order to conclude that someone is protected," says Innis. The GSK field trial will provide the first data directly relating antibody production to disease protection.

Because of the slow progress with live attenuated vaccines, researchers have been working on alternatives. The furthest along is a chimeric vaccine that uses a yellow fever vaccine virus as a backbone but replaces several key structural genes with dengue counterparts. The technique was pioneered at Saint Louis University in Missouri, further developed by the company Acambis in Cambridge, Massachusetts, and Cambridge, U.K., and finally licensed to Sanofi Pasteur, which now has a tetravalent vaccine in phase II clinical trials in adults and children.

Researchers say there is merit in both approaches. One advantage of chimeric vaccines, says Gubler, is that researchers can genetically manipulate them to fine-tune the degree of attenuation. A downside, adds Innis, is that such recombinant vaccines have just a few of the wild-type dengue genes, whereas the live attenuated vaccines have all 10 genes for each component, possibly making them more efficacious. "The real question is 'What works?' " says Barrett, who expects some answers to come out of the ongoing trials.

CREDIT: JAMES GATHANY/CDC

The Dengue Vaccine Pipeline

Mahidol University/Sanofi Pasteur: Live attenuated vaccine; work halted after phase II clinical trials of a tetravalent vaccine

Walter Reed Army Institute of Research/GlaxoSmithKline: Live attenuated vaccine; tetravalent formulations in phase II clinical trials

Acambis/Sanofi Pasteur: Live chimeric vaccine with dengue genes added to an attenuated yellow fever virus; tetravalent formulations in phase II clinical trials

U.S. National Institute of Allergy and Infectious Diseases: Live chimeric vaccine with dengue-1, -2, and -3 genes added to an attenuated dengue-4 virus; monovalent formulations in phase I and II trials

U.S. Naval Medical Research Center: DNA vaccine based on dengue genes; monovalent vaccine for dengue 1 in phase I trials

Hawaii Biotech: Subunit vaccine containing dengue viral proteins; human trial now being planned

As these and other candidate dengue vaccines (see table, above) wend their way through early-stage clinical trials, the Pediatric Dengue Vaccine Initiative (PDVI) in Seoul, South Korea, is using the Gates grant to ready field sites for the large-scale phase III trials that will be needed to license a vaccine. Even before trials start, baseline data on field trial sites are needed, which require laboratories and staffs conducting ongoing surveillance of the dengue viruses in circulation and collecting epidemiological data such as infection rates. All vaccines face this hurdle, but dengue's is a bit higher because researchers must distinguish and track the four dengue viruses. PDVI Director Harold Margolis says "it will be difficult" to show efficacy against all four serotypes with trials at just one site, because one virus usually predominates in a region. Trials may have to be done at multiple sites, although researchers and regulators are still pondering the best approach. PDVI is also working on standardizing laboratory diagnostic protocols and clinical case definitions to support clinical trials.

Gubler, who chairs PDVI's board of counselors, says, "This saves the manufacturers a lot of time and a lot of money [because] they don't have to develop these field sites themselves." He believes this logistical help has encouraged smaller firms with novel approaches to take up the dengue vaccine challenge and thinks it may shave 3 years off development time. Now all they need are some phase III candidates, which Gubler and others predict should come along well within the next 10 years.

–DENNIS NORMILE

LETTERS

edited by Etta Kavanagh

Why Do Team-Authored Papers Get Cited More?

IN THEIR REPORT "THE INCREASING DOMINANCE OF TEAMS IN PRODUCTION OF KNOWLedge" (18 May, p. 1036), S. Wuchty *et al.* observe that references with multiple authors receive more citations than solo-authored ones. They conclude that research led by teams has more quality than solo-led research, but inappropriate control of confounding (including confounding by publication type) makes several alternative explanations plausible. The Institute for Scientific Information (ISI) Web of Science database includes not only original research but also editorials and letters to the editor (*1*). This kind of scientific literature is both more frequently authored by just one or two researchers and less frequently cited. Significantly, it would also be consistent with the observed relationship between citations and actual team size.

More importantly, there are several ways a larger group of authors can influence the number of citations of their common work, beyond the quality of the paper. We can think of a reference by n authors as having n times more proponents than a solo-authored one. This would include self-citations in other papers (as already observed in the study), citations in other kinds of scientific literature, and an increased number of research groups being familiar with the article. Moreover, scientific communication is not limited to journals. The longer the author list is, the greater the probability of the paper being presented to several conferences is, especially if the team is multidisciplinary.

Linking organizational features of research with the quality of its output is of utmost importance, because it will eventually provide policy-makers and funding bodies with hard evidence for the prioritization of specific features of research proposals. We should therefore be extremely cautious when interpreting this kind of study.

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Reference

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IN DEMONSTRATING THE INCREASING DOMInance of teams in academic and patent publishing, Wuchty *et al.* use a circular argument regarding scientific progress, defining impact as "the number of citations each paper and patent receives." Technically speaking, the number of citations reflects popularity, not necessarily quality.

In academic publishing, authors clearly copy the citations from other papers (*1*). The resulting frequency dependence in citation rate means that citations of a successful paper increase geometrically, with crucial dependence on initial conditions (*2*). An effective strategy, therefore, is quite similar to product marketing (*3*): Try to get noticed at the beginning and then hope the process will take over through frequency-dependent copying. Co-authoring with a well-known researcher clearly helps in this respect (*4*), but larger teams also have an inherent advantage in their ability to "seed" the process soon after publication through self-citation as well as citation by a larger network of colleagues.

With copying underlying much of popular cultural change (*5*), the real question is, how does number of citations relate to quality? One of the studies that Wuchty *et al.* cite even reports that "citations are not a reliable indicator of scientific contribution at the level of the individual article" (*6*). With pop music, for example, the opportunity to view (and copy) other people's choices leads to drift in the most downloaded songs (*7*), such that popularity and quality become decoupled. How can we assume academic citation is so different?

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WUCHTY *ET AL.* FOUND THAT FROM 1955 TO 2000, the relative citation rate for publications with multiple authors increased across a broad range of academic disciplines. The Relative Team Impact (RTI) citation statistics presented in their Fig. 2, however, seem to be for entire teams. Dividing by mean team size shows that relative per capita citation rate for teams fell by over a third over this 45-year period, compared to solo authors, for science and social science. The only exception is arts and humanities, where teams are rare in any case. If citation rates measure performance, then on average, researchers still perform better when they work alone. The main payoff from joining a team is increased odds of a very heavily cited publication.

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WUCHTY *ET AL.* EXAMINE THE GROWTH OF collaborative research in a variety of scientific fields and how it has affected the quality of research. They found that research produced collaboratively is of a higher quality, as measured by citations, than research reported in

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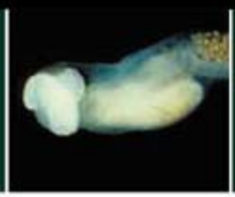
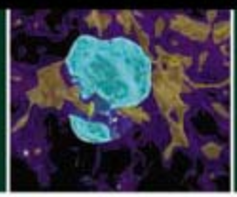


Deciphering microbial activity

1510



First light from filaments

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single-author articles. They argue that although "the increasing capital intensity of research may have been a key force in laboratory sciences where the growth in teamwork has been intensive… it is unlikely to explain similar patterns in mathematics, economics, and sociology, where we found that growth rates in team size have been nearly as large" (p. 1038). I offer an explanation for the increase in collaborative research in the social sciences (*1*). I argue that we are seeing more collaborative work in the social sciences because there are selection pressures on those who do not collaborate. Given that collaborative research is generally of a higher quality, and careers in the sciences are profoundly affected by the quality of one's research, scientists who are not prepared to collaborate are becoming a smaller portion of the population of researchers, even in the social sciences. Those who are unwilling or unable to collaborate are being weeded out at a higher rate than those willing and able to collaborate.

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Response

BUILDING ON OUR FINDINGS THAT (I) *SCIENCE* has made a nearly universal shift toward teamwork and (ii) highly cited research is now more frequently produced by teams rather than solo authors, the Letter writers raise questions regarding mechanisms and interpretations.

One question is whether citation rates reflect a paper's quality. Valderas and Bentley suggest that team-authored papers receive more citations than solo-authored papers because of a team advantage for self-promotion. Although citations gained are likely a function of both a paper's scientific contribution and marketing, several reasons suggest that self-promotion modestly affects citation rates on balance.

First, our paper presented analysis with self-citations included and with self-citations removed (always excluding the editorials and letters to the editor that concern Valderas). The results change little when self-citations are excluded, suggesting that the team citation advantage holds even without self-promotion. Second, a self-promotion argument does not explain the team citation advantage for patents, where citation decisions are primarily made by disinterested third-party experts (*1*). Third, we find that the team citation advantage over solo-authored papers is growing over time for teams of any fixed size, yet a self-promotion argument suggests a static team advantage, not an increasing one. Finally, Bentley cites Salganik *et al.* (*2*) as evidence that "bad" songs (i.e., by analogy, weak papers) can be turned into a hit

through false buzz about the song, a process that could be created in scientific circles through self-promotion. However, Salganik *et al.* (*2*) demonstrate that this effect works only on a song-by-song basis. When average effects are examined, average popularity and average quality are highly correlated. Our measures of average citations taken over large numbers of papers would then appear to be a reasonable measure of scientific influence.

More generally, we avoided the term "quality" and used the broader constructs of "impact" and "influence" to construe the meaning of a paper's citation rate. A paper that is high "quality" by some standard (functional contribution, breadth of application, timelessness, elegance, etc.) will typically have little impact if it is not cited.

Our analysis focuses on impact at the paper level. Buckley is interested in the impact of individual authors. He attempts to infer individual impact from our paper-level analysis, but this inference is not possible without knowledge of the amount of time each author contributes per paper. His implicit assumption is that a paper with N authors requires N times as much collective effort as a solo-authored paper. A more unexceptionable assumption may be that multi-authored papers require less effort per person, which would explain the prevalent observation that people who tend to write in teams tend to write more papers. With higher rates of publication, team authorship may be associated not just with more citations, but more citations per unit of author's time. Nevertheless, assessment of the impact of individual authors requires data on time inputs, an important direction for future work.

Wray provides a possible interpretation for why scientists work in teams. As we noted in our paper, there are many possible mechanisms behind the universal structural shift toward teams in science, and we look forward to future work that assesses and disentangles potential causes.

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Coral Reefs Still in Danger from Tourism Head

AS A DIVER SINCE 1985 WITH OVER 500 DIVE hours logged on tropical reefs and now a coral reef conservationist working directly with the marine tourism sector, I have to wonder if Norman Karin is talking about the same dive community I know ("A diver's perspective on coral damage," Letters, 13 July, p. 196).

I'm not about to pretend that recreational use and overuse ranks with climate change, coastal development, and unsustainable and destructive fishing practices as the most significant global threats to coral health. And I've had the honor to dive with stellar dive businesses who are ambassadors for sustainability. But to suggest that the dive community as a whole has had some sort of collective epiphany around sustainable behavior and best practices is just uninformed.

According to a 2002 report (*1*), marine tourism is a major factor contributing to reef decline at no-take Marine Protected Areas (MPAs) in Hawaii. In 2003, between 28,000 and 100,000 people per year visited just four

sites, with diving and snorkeling being the most popular marine recreation activity (*2*). Tourism numbers have increased steadily over the years. In 1999, tiny Honolua Bay on Maui averaged 250 tourists per day and up to 700 per day during peak season (*3*). This volume has certainly increased. Research also shows that 45% of certified SCUBA divers who visit dive sites break coral colonies. Most of this damage appears to be from fin kicks (*4*).

Finally, Karin points to Bonaire Marine Park as evidence of diver awareness. I agree that Bonaire is spectacular and a model that should be emulated and exported worldwide. But to hold up the well-funded, relatively affluent, politically stable, and uncorrupt Netherlands Antilles as somehow representative of most coral reef destinations and MPA systems is disingenuous. Most MPAs are not reaching their conservation goals. Crushing poverty and competing resource use often derail the best conservation efforts. Denial or special pleading to displace tourism's contribution and responsibility certainly doesn't help.

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TECHNICAL COMMENT ABSTRACTS

COMMENT ON "The Consensus Coding Sequences of Human Breast and Colorectal Cancers"

William F. Forrest and Guy Cavet

Sjöblom *et al.* (Research Article, 13 October 2006, p. 268) used data from cancer genome resequencing to identify genes with elevated mutation rates. Their analysis used point probabilities when it should have used *P* values for the hypotheses they intended to test. Reimplementing their analysis method with exact *P* values results in far fewer genes with mutation rates that achieve statistical significance.

Full text at www.sciencemag.org/cgi/content/full/317/5844/1500a

COMMENT ON "The Consensus Coding Sequences of Human Breast and Colorectal Cancers"

Gad Getz, Holger Höfling, Jill P. Mesirov, Todd R. Golub, Matthew Meyerson, Robert Tibshirani, Eric S. Lander

Sjöblom *et al.* (Research Article, 13 October 2006, p. 268) reported nearly 200 novel cancer genes said to have a 90% probability of being involved in colon or breast cancer. However, their analysis raises two statistical concerns. When these concerns are addressed, few genes with significantly elevated mutation rates remain. Although the biological methodology in Sjöblom *et al.* is sound, more samples are needed to achieve sufficient power.

Full text at www.sciencemag.org/cgi/content/full/317/5844/1500b

COMMENT ON "The Consensus Coding Sequences of Human Breast and Colorectal Cancers"

Alan F. Rubin and Phil Green

Sjöblom *et al.* (Research Article, 13 October 2006, p. 268) reported many new genes with an apparent significant excess of mutations in breast and colorectal cancer. Reanalysis of their data with more appropriate statistical methods and background mutation rate assumptions reveals that few if any of these genes have significantly elevated mutation rates.

Full text at www.sciencemag.org/cgi/content/full/317/5844/1500c

RESPONSE TO COMMENTS ON "The Consensus Coding Sequences of Human Breast and Colorectal Cancers"

Giovanni Parmigiani, Jimmy Lin, Simina M. Boca, Tobias Sjöblom, Siân Jones, Laura D. Wood, D. Williams Parsons, Thomas Barber, Phillip Buckhaults, Sanford D. Markowitz, Ben Ho Park, Kurtis E. Bachman, Nickolas Papadopoulos, Bert Vogelstein, Kenneth W. Kinzler, Victor E. Velculescu

Forrest and Cavet, Getz *et al.*, and Rubin and Green describe a variety of statistical methods to analyze the mutational data published in Sjöblom *et al.* However, their conclusions are inaccurate because they are based on analyses that do not fully take into account the experimental design and other critical features of our study. When these factors are incorporated, their methods provide estimates similar to those we reported and support the conclusion that a large number of genes are mutated at rates greater than the passenger mutation rate.

Full text at www.sciencemag.org/cgi/content/full/317/5844/1500d

Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 3 months or issues of general interest. They can be submitted through the Web (www.submit2science.org) or by regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

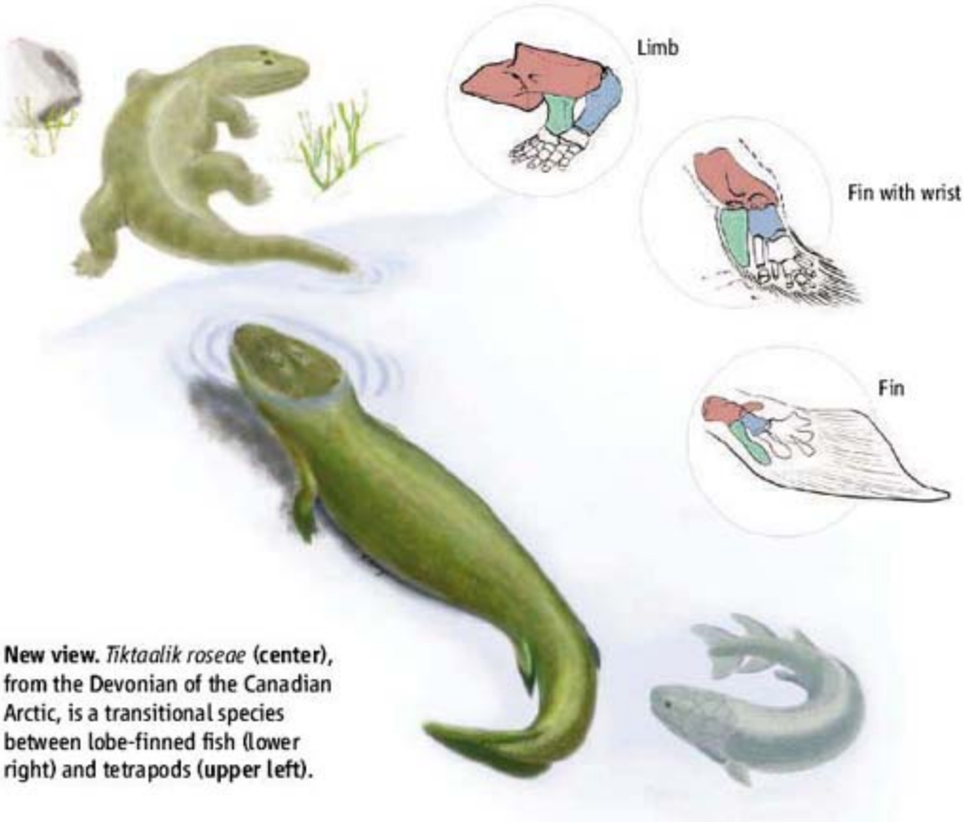
EVOLUTION

Putting the Pieces Together

Alan C. Love

Fins into Limbs
Evolution, Development, and Transformation
by Brian K. Hall, Ed.
University of Chicago Press, Chicago, 2007. 459 pp. $110, £69.50. ISBN 9780226313368. Paper, $45, £28.50. ISBN 9780226313375.

The completion of a jigsaw puzzle brings tremendous satisfaction; however, a few missing pieces lead to considerable frustration. Having the intended picture of a puzzle on the container contributes to the satisfaction (or the frustration). But what about a puzzle where there is no master picture to guide the reconstruction? How do you know if you have all the pieces? And what if the contours of some pieces are unclear, making it difficult to see how they fit together? Such is the lot of biologists attempting to explain key evolutionary transitions in the history of life.



New view. *Tiktaalik roseae* **(center), from the Devonian of the Canadian Arctic, is a transitional species between lobe-finned fish (lower right) and tetrapods (upper left).**

Fins into Limbs is an exploration of a long-standing evolutionary puzzle associated with the origin of tetrapods and the vertebrate invasion of land. Brian Hall has assembled a stellar array of contributors from various fields that represent the pieces necessary for a solution. The volume is handsomely executed and also timely. It collects a diverse body of recent research on fins and limbs emerging from evolutionary developmental biology (evo-devo), functional morphology, and paleontology, all of which have transformed our conception of what the fin-limb transition looked like. Instead of a lobe-finned fish hauling itself up onto the sand, we have a much different image of the evolutionary transformation (*1*). Recent papers that could not be incorporated in the volume have revealed new transitional fossils (*2*) and continued to augment our understanding of the molecular genetic mechanisms of limb development (*3*).

The volume's first part, Evolution, provides historical background on the fin-to-limb puzzle and paired appendage locomotion, as well as a phylogenetic context informed by paleontology. The origin of the autopodium (hand/foot)—encapsulated in Hall's pithy slogan "fins minus fin rays plus digits equal limbs"—is analyzed from an evo-devo perspective. In the second part, Development, an overview of fin and limb ontogeny is followed by treatments of chondrogenesis, osteogenesis, apoptosis, joint formation, postnatal growth, and regeneration. The third part, Transformation, addresses the subsequent fate of tetrapod limbs, including the appendicular skeleton of amphibians, digit and limb reduction in reptilians, mammalian limb diversity, and skeletal adaptations for flight, digging, and swimming. These later chapters are not pieces of the puzzle themselves as much as investigations of other evolutionary transitions of tetrapod appendages relevant to understanding how the different pieces fit together when explaining the origin of innovations.

Although the lengths of the contributions vary substantially, the more interesting variation lies in the styles they exhibit: anatomical, functional morphological, and molecular genetic. Very few chapters bring these considerations together, and even the contrast among cognate entries is striking. Chondrogenesis and osteogenesis in fins are treated in terms of histology, whereas the entry on limbs grants priority to molecular genetics. The influence of model organisms (zebrafish, chicken, and mouse), chosen for different scientific puzzles (such as isolating key processes underlying how an organism develops from embryo to adult), is also apparent. My favorite was the last chapter, by Matthew Vickaryous and Wendy Olson, on the curiosity of sesamoids and ossicles in the appendicular skeleton. The combination of a topic nearly untouched by other contributors and an explicit blending of the different styles makes it a gem.

Specialists will no doubt question particular interpretations within individual chapters, but the book's significance lies in the overarching outlook on the fins-into-limbs puzzle. Attacking the thorny empirical and conceptual questions that compose this problem requires multiple disciplinary approaches, each with specialized concepts and methods. Sometimes this introduces potential communication difficulties (e.g., the developmental "mesomere" of vertebrate mesoderm and anatomical "mesomeres" in pectoral fins), and the substantial differences in terminology are on full display. But do we have all the disciplinary pieces to the puzzle? The volume lacks discussions from evolutionary genetics and (paleo)ecology, which encourages a complaint that evolution plays second fiddle to comparative development in it. Some might disagree with claims about the evolutionary process, such as patterns of genetic regulatory elements pointing "to changes in a region-

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specific regulatory sequence as being the mechanism for evolutionary change." As the editor acknowledges, this book is focused on skeletal elements, which is his area of expertise (*4*). Thus, musculature, innervation, vasculature, and other features are relegated to the background, although some of these missing pieces can be found elsewhere (*5*).

Knowing how the pieces fit together is a more difficult question. The contributors make little effort to integrate the research from different approaches. One author notes that "the challenge is to continually synthesize knowledge gained from multiple perspectives into an ever more refined understanding." In some cases, this synthesizing is studiously avoided, and at other points, there is inadvertent stumbling over borrowed concepts. (An exception is Gunter Wagner and Hans Larsson's discussion of evolutionary novelties, with its explicit fusion of anatomy, phylogeny, development, and evolution.) But this is not the fault of the editor or contributors. It is symptomatic of the complex structure of biological knowledge. Multidisciplinary research on evolutionary problems may be essential, but the nature of its composition and functioning remains elusive.

Fins into Limbs serves as a necessary reference and a worthy guide to future research on this and other evolutionary transitions. It tells us what we know, what we don't know, and what we'd really like to know. Thus it points us in the direction of which pieces are required to solve the puzzle and reminds us of the pressing need to figure out how they all fit together.

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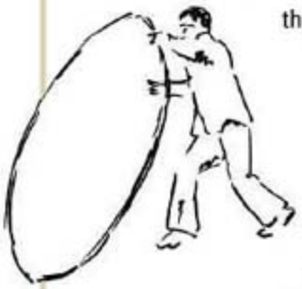
THE GONZO SCIENTIST

A Summer Camp for Grown-Ups

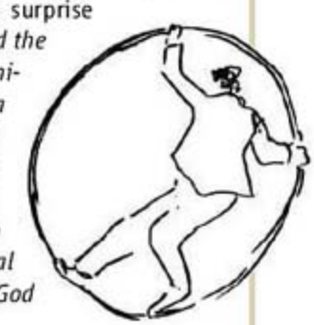
WHEN I WAS 11 YEARS OLD, I went to summer camp for geeks. The goal was to learn how to program computers, but more importantly, I discovered a new world of like-minded people. So I was thrilled to learn that such summer camps aren't just for kids anymore. From the TED conference and the Aspen Ideas Festival to the Google Science Foo Camp, there are now more grown-up summer camps than you can shake a marshmallow on a stick at. This summer, *Science* sent me to investigate one of these: *idea*City in Toronto, Canada.

For a full account, see www.sciencemag.org/sciext/gonzoscientist

The event mostly focused on how scientific ideas can make the world a better place. The list of 50 speakers reads like a Who's Who of science, technology, and the arts. They included David Schurig, the Duke University physicist who co-invented an invisibility cloak last year; John Polanyi, Nobel laureate and chemical kinetics pioneer; Frans de Waal, the Emory University ethologist who is uncovering the biological roots of morality; Étienne Baulieu, the inventor of the morning-after pill; and even Brian Shuster, CEO of redlightcenter.com—an online universe similar to Second Life but with cybersex and virtual drugs. With such a diversity of thinkers (not all academics) on the podium and in the audience, there were plenty of productive, even amusing, interactions—and some sharp disagreements.



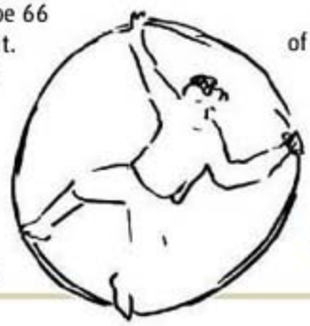
During one session, I witnessed the verbal equivalent of a professional wrestling match between Richard Dawkins and the celebrity rabbi Shmuley Boteach. Dawkins stepped into the ring first. The wily Oxford professor of popular science may be 66 years old, but he can handle himself in a fight. He's lean, fast on his feet, and he wears silky suits that are hard to grip. His opening was by the book, first maneuvering to put the fight on his own terms. Scientific arguments will get you nowhere in a God rumble unless you can establish that science has something to say about religious matters. A long and circling mini-lecture on the anthropic principle did the job. Then, to get at the throat, he made a big flying leap: *Scientific laws as we understand them should apply to God.* And then came Dawkins's surprise attack: *To have created the Earth, let alone the universe, God must be a vastly more intelligent and complex being than we are. Our own excellence in design is already the vastly improbable result of natural selection. Ergo, by the laws of probability, God almost certainly doesn't exist.*



A bearded man swaggered onstage and the game was on. Rabbi Shmuley deployed a fighting style perfected by "Rowdy" Roddy Piper, the Canadian kilt-wearing wrestler. During Piper's legendary feuds with Hulk Hogan and Mr. T, he famously exclaimed, "Just when they think they got answers, I change the questions!" And that's just what the rabbi did. His opening was actually a double attack, starting with a classic Piper eye-poke: *Dawkins says that he has a problem with religion because it's not true. He lives in England where they have a queen, but he hasn't attacked the royal family. Is it true that some people are born more special than others?* Then, taking advantage of the momentary distraction created by this dubious statement, the rabbi followed with a savage foot stomp: *Dawkins is married, so presumably he believes in the institution of marriage. But is marriage a true institution? According to evolution, love is a trick played on the mind to ensure that you have sex and propagate the species. Dawkins says he doesn't believe in love. And most evolutionary biologists don't either.* There was a lot more on both sides.

Of course, the real show is always afterward, when the fight spills out of the ring.

– JOHN BOHANNON



To find out more and follow our intrepid reporter into a jungle of space tourism, eco-warriors, robots, pandemics, and even belly dancing, we invite you to turn to the first installment of the Gonzo Scientist, an approximately monthly adventure chronicled at www.sciencemag.org/cgi/content/full/317/5844/1495b.

10.1126/science.1149843

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CLIMATE CHANGE

The Limits of Consensus

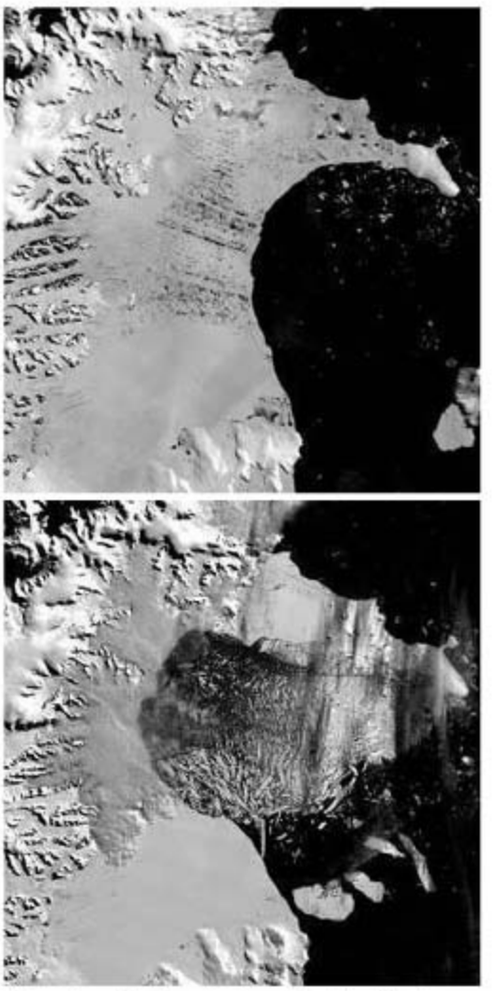
The establishment of consensus by the IPCC is no longer as critical to governments as a full exploration of uncertainty.

Michael Oppenheimer,[1,2]* Brian C. O'Neill,[3,4] Mort Webster,[5] Shardul Agrawala[1,6]

The Intergovernmental Panel on Climate Change (IPCC) has just delivered its Fourth Assessment Report (AR4) since 1990. The IPCC was a bold innovation when it was established, and its accomplishments are singular (*1*, *2*). It was the conclusion in the IPCC First Assessment Report that the world is likely to see "a rate of increase of global mean temperature during the next century … that is greater than seen over the past 10,000 years" (*3*) that proved influential in catalyzing the negotiation of the United Nations Framework Convention on Climate Change. The conclusions of the Second Assessment with regard to the human influence on climate (*4*) marked a paradigm shift in the policy debate that contributed to the negotiation of the Kyoto Protocol. IPCC conclusions from the Third, and now the Fourth, assessments have further solidified consensus behind the role of humans in changing the earth's climate.

The emphasis on consensus in IPCC reports, however, has put the spotlight on expected outcomes, which then become anchored via numerical estimates in the minds of policy-makers. With the general credibility of the science of climate change established, it is now equally important that policy-makers understand the more extreme possibilities that consensus may exclude or downplay (*5*).

For example, the Working Group I (WGI) "Summary for Policymakers" (SPM) of AR4 anticipates a rise in sea level of between 18 and 59 cm by the year 2100 (*6*), a "model-based range" composed largely of thermal expansion of oceans, melting of nonpolar glaciers, and the gradual response of ice sheets. The range does not include the potential for increasing contributions from rapid dynamic processes in the Greenland and West Antarctic ice sheets (WAIS), which have already had a significant effect on sea level over the past 15 years and could eventually raise sea level by many meters. Lacking such processes, models cannot fully explain observations of recent sea-level rise, and accordingly, projections based on such models may seriously understate potential future increases. Although the AR4 SPM recognizes the possibility of a larger ice-sheet contribution, its main quantitative results indicate the opposite: Uncertainty in sea-level rise is smaller, and its upper bound is lower, for the 21st century than was indicated in the Third Assessment Report (*7*). On the related question of sea-level rise beyond the 21st century, whereas the Third Assessment's SPM provided a numerical estimate of a potential contribution from WAIS, the AR4 WGI SPM doesn't mention WAIS at all. This omission presumably reflects a lack of consensus arising from the inadequacy of ice-sheet models for WAIS made so apparent by recent observations.



Not captured by ice-sheet models. (Top) The Larsen B ice shelf along the Antarctic Peninsula on 31 January 2002. **(Bottom)** A large section has disintegrated, 5 March 2002. Glaciers behind the collapsed section of the ice shelf subsequently accelerated their discharge into the ocean, apparently because of the loss of buttressing by the ice shelf. Neither rapid collapse nor buttressing are captured by ice-sheet models, and both could substantially affect the rate of future sea-level rise as larger ice shelves to the south in West Antarctica warm (*26*).

CREDIT: NATIONAL SNOW AND ICE DATA CENTER, BOULDER, CO

Nevertheless, alternatives to model-based approaches, such as empirical analysis and expert elicitation, were available for exploring uncertainty in 21st-century (*8*) and long-term sea-level rise (*9*), respectively. Such information certainly would have been useful to policy-makers, particularly for WAIS, which contains enough ice to raise sea level by about 5 m.

Setting aside or minimizing the importance of key structural uncertainties in underlying processes is a frequent outcome of the drive for consensus (*5*, *10*). For example, ranges of projected warming and atmospheric composition in AR4 include an amplifying effect of interactions between climate and the carbon cycle. However, the estimated uncertainty in this effect is based largely on models that omit a number of poorly understood processes (*11*), such as feedbacks on carbon contained in permafrost; changes in marine ecosystem structure; and responses to land-use history, nutrient limitation, and air-pollution effects. These models also share similar assumptions about the temperature sensitivity of carbon fluxes from soils based on experimental results that cannot be reliably scaled to the ecosystem level (*12*). A fuller accounting of uncertainty would be more appropriate.

Similarly, the narrowing of uncertainty (relative to previous assessments) associated with potential changes in the meridional overturning circulation relies on agreement across models, but the structural uncertainty in all the models means that less may be known than suggested by the numerical estimates (*13*).

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The views expressed in this paper are those of the authors and not necessarily those of the institutions they are affiliated with.

Like models of physical processes, conclusions drawn on the basis of socioeconomic models may also be subject to premature consensus. Estimates of the costs of mitigating emissions come primarily from models that omit endogenous technical change, a poorly understood process. This omission could cause a significant bias, not only in mitigation costs, but also in the stringency of near-term mitigation that may be justified for a given damage function or stabilization target (*14*–*16*). Similarly, the conventional use of the range of emissions described by the IPCC Special Report on Emissions Scenarios (SRES) marker scenarios as a key determinant of uncertainty in projecting climate change, sea-level rise, impacts, and mitigation costs may be misguided. The SRES scenarios were intended to be representative of scenarios available in the literature at the time they were produced, with no explicit goal of spanning the full range of uncertainty. The SRES assessment made no attempt to judge whether emissions pathways outside the range it covers could plausibly occur. In fact, pathways outside that range were known at the time, and more have been developed since the publication of SRES (*17*).

To be sure, the underlying IPCC chapters do detail the limitations and uncertainties associated with such conclusions. But the caveats are often cryptic or lost entirely in the highly influential SPMs. This inevitably leads to an anchoring by both policy-makers and scientists around any numerical estimates that are reported in these summaries.

Ignoring the implications of structural uncertainty in models of key aspects of the climate system is reminiscent of the way assessments treated the uncertainty in ozone photochemical models. Projections of ozone depletion were made from 1974 onward based on improved understanding of gas-phase chemistry (*18*). Knowledge of stratospheric chemistry was then transformed by the report in 1985 of large, seasonal Antarctic depletion (the "ozone hole"); the validation in 1987 of its origin in halogen photochemistry; and subsequent identification of depletion at the mid-latitudes and in the Arctic (*19*, *20*). Various heterogeneous chemical reactions, discounted by most researchers years before and absent from nearly all model simulations (*21*), were shown to be the missing photochemical processes required to explain observed depletion. Their potential implications were of concern to some scientists (*22*), but this structural uncertainty was generally downplayed in assessments until the ozone hole was reported.

Avoiding Premature Consensus

The IPCC has made progress over four assessment cycles in its treatment of uncertainties. However, this progress is limited and uneven across its Working Groups. Several additional modifications to the current practice could reduce the risk of ignoring or underemphasizing critical uncertainties.

First, given the anchoring that inevitably occurs around numerical values, the basis for quantitative uncertainty estimates provided must be broadened to give observational, paleoclimatic, or theoretical evidence of poorly understood phenomena comparable weight with evidence from numerical modeling. In areas in which modeling evidence is sparse or lacking, IPCC sometimes provides no uncertainty estimate at all. In other areas, models are used that have quantitatively similar structures, leading to artificially high confidence in projections (e.g., in the sea-level, ocean-circulation, and carbon-cycle examples above). One possible improvement would be for the IPCC to fully include judgments from expert elicitations (*23*), as Working Group II has sometimes done. Beyond this, increased transparency, including a thorough narrative report on the range of views expressed by panel members, emphasizing areas of disagreement that arose during the assessment, would provide a more robust evaluation of risk (*24*). It would be critical to include this information not only in the chapters, but in the summaries for policymakers as well.

Second, IPCC should revise its procedure for expert review to guard against overconfidence. External reviewers should ferret out differences between chapters or author subgroups, and a special team of authors could be instructed to examine the treatment of unlikely but plausible processes, perhaps in a separate chapter. Integration of risk assessment across Working Groups in advance of drafting of the Synthesis Report would highlight internal discussions and disagreements. At the end of an assessment cycle, a small external team of ombudsmen should review key problematic issues (of a scientific nature) that may have emerged from the report and should recommend modifications of approaches for handling these areas in subsequent reports.

Third, IPCC could also formalize a process of continuous review of its structure and procedures. A useful example is provided by the history of IPCC emissions scenario development, which included a series of reviews for production of the SA90, IS92, and SRES scenarios (*25*).

Fourth, and perhaps most important, national governments now need to confront a more fundamental question of how often they need comprehensive assessments of climate change. Addressing the special risks entailed in particular aspects of the climate system, like the ice sheets or carbon cycle, might be better approached by increasing the number of concise, highly focused special reports that can be completed relatively quickly by smaller groups, perhaps even by competing teams of experts. At this juncture, full assessments emphasizing consensus, which are a major drain on participants and a deflection from research, may not be needed more than once per decade.

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IMMUNOLOGY

Square-Dancing Antibodies

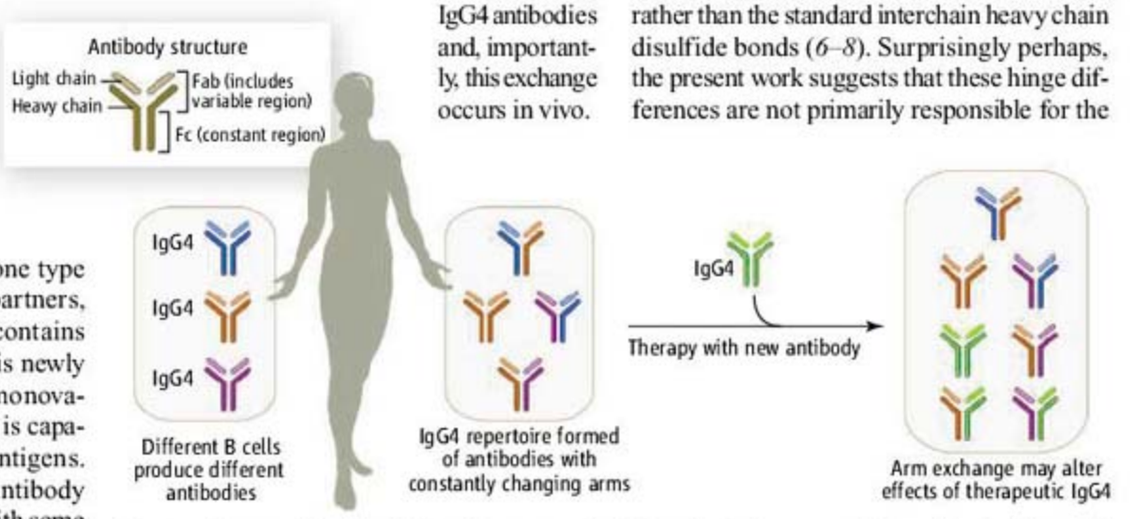
Antibody therapies need to take account of a subclass of immunoglobulin G that can swap subunits in vivo.

Dennis R. Burton and Ian A. Wilson

Antibodies are among nature's most versatile molecules. The classic Y-shaped molecules can recognize essentially any antigen by the variable tips of the Fab (fragment antigen binding) arms, whereas the Fc (fragment crystallizable) stem recognizes effector molecules that help eliminate antigen (see the figure). The two Fab arms are identical, allowing antibodies to bind bivalently to repeating antigens on, for example, microbial pathogens or tumor cells. This arrangement enhances the affinity of antibody for antigen and allows antibodies to cross-link antigen molecules under certain conditions. Identity of the Fab arms is expected because an antibody is a tetramer of two identical dimers. However, on page 1554 in this issue (*1*), van der Neut Kolfschoten *et al.* show that one type of antibody can exchange dimer partners, generating a hybrid antibody that contains two different Fab arms. Although this newly formed antibody can only bind monovalently, even to a repeating antigen, it is capable of cross-linking two different antigens. The consequences of such hybrid antibody formation are very interesting, but with some potentially serious ramifications.

The antibody molecule that exchanges Fab arms is human immunoglobulin G4 (IgG4). IgG, the predominant antibody in the serum, consists of four subclasses in humans. The least abundant subclass is IgG4, which is present in serum at a concentration of about 0.1 to 0.5 mg/ml (*2*). The IgG subclasses differ most in their Fc regions, and IgG4 notably has an Fc that interacts poorly with effector systems of the immune response, such as complement and Fc receptors expressed by certain white blood cells. This property has made IgG4 a favorite for therapeutic applications in which antibody is required to bind to a target, but not trigger effector activities.

Previously, it was noted that sera from donors making IgG4 antibodies to both house dust mite and grass pollen can cross-link these two antigens, whereas sera from donors that make antibodies to one antigen alone cannot (*3*). Further, whereas most IgG molecules precipitate antigens when mixed in the right proportions, IgG4 antibodies do not (*4*). Some interesting hypotheses (*5*) were advanced to interpret these data, but this new study convincingly explains the behavior of IgG4. In particular, addition of a reducing agent, such as reduced glutathione, promotes exchange of Fab arms in vitro for both polyclonal and monoclonal IgG4 antibodies and, importantly, this exchange occurs in vivo.



Partners in arms. (Top) The Y-shaped structure of an IgG molecule is composed of two identical heavy (H) chains and two identical light (L) chains, resulting in two identical antigen-binding sites at the tips of the Y. However, an H-L unit of one IgG4 molecule can exchange with that of another IgG4 to produce a hybrid molecule with different antigen specificities. Because the Fc parts of two IgG4 molecules are identical, their Fab arms are effectively swapped. **(Bottom)** The exchange of Fab arms between IgG4 molecules is dynamic. An initially homogeneous IgG4 antibody, when administered to a human, will begin swapping arms. Partners exchange constantly, as this "dance" progresses.

How then does this exchange of Fab arms occur between IgG molecules? Dimerization of IgG heavy chains is thought to be driven by the pairing of the third constant domain (C_H3) of each heavy chain. This pairing is usually stabilized further by interheavy chain disulfide bridges *some* distance away in *the* hinge region. In IgG4, the hinge region has the amino acid sequence Cys-Pro-Ser-Cys, compared to Cys-Pro-Pro-Cys in IgG1, and this difference has been linked to a tendency of IgG4 to form novel intrachain disulfides in the hinge region rather than the standard interchain heavy chain disulfide bonds (*6*–*8*). Surprisingly perhaps, the present work suggests that these hinge differences are not primarily responsible for the exchange of Fab arms but, instead, implicates the C_H3 domains.

An insightful application of this Fab arm exchange is illustrated in a monkey model of the human autoimmune disease myasthenia gravis. The disease presents as muscle weakness associated with autoantibodies to acetylcholine receptors (AChR) expressed on muscle cells. van der Neut Kolfschoten *et al.* show that a human IgG1 antibody to AChR isolated from a patient with myasthenia gravis induces disease symptoms in monkeys presumably by cross-linking AChR molecules. However, a human IgG4 antibody with identical binding properties to AChR as the IgG1 antibody does not cause disease. Furthermore, the IgG4 antibody protects against IgG1-mediated disease likely by displacing IgG1 and binding monovalently to AChR.

Sequence differences in the C_H3 domain of IgG4 and IgG1 are limited to four residues; most notably, an arginine at position 409 at the interface between C_H3 domains in IgG4 is replaced by a lysine in IgG1, and this may be crucial for Fab arm exchange. Although this appears to be a rather conservative mutation, arginine-to-lysine substitutions can have large effects on protein-protein interactions in other systems (*9*, *10*). Clearly, further mutagenesis studies are warranted to address this possibility.

What are the ramifications of Fab arm exchange for antibody-mediated immunity? IgG4 is produced particularly in response to high doses of protein antigen, and there has been controversy over the abil-

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ity of IgG4 to dampen IgE responses when the antigen is an allergen and also whether this dampening effect has clinical utility (*5*, *11*). Any effects are likely due to competition between IgE and IgG4 to bind antigen, but this should now be considered in the light of the findings of van der Neut Kolfschoten *et al.*

Several IgG4 molecules are in clinical use or in clinical trials. In some instances, the hinge region of IgG4 has already been "stabilized" by mutation to the IgG1 Cys-Pro-Pro-Cys sequence, and it is probable that Fab arm exchange has been reduced or even abrogated. In other instances, a wild-type IgG4 molecule may have been used, and the possibility that Fab arm exchange could contribute to adverse effects in IgG4 therapy (*12*, *13*) should be explored immediately.

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GEOCHEMISTRY

New Players in an Ancient Cycle

Isotope data from Australia provide evidence for the existence of bacteria that used elemental sulfur in metabolic processes about 3.5 billion years ago.

Bo Thamdrup

Microorganisms such as cyanobacteria, sulfate reducers, and methane-producing archaea can be traced back to ~2.7 billion years ago on the basis of chemical biomarkers, microfossils, and stable isotopes. Farther back in time, the evidence for microbial metabolism resembles a puzzle in which most pieces are missing. On page 1534 of this issue, Philippot *et al.* (*1*) present a new piece: isotopic evidence for sulfur disproportionation, a little-explored metabolic process, in a 3.5-billion-year-old marine deposit.

The geological record of stable sulfur isotopes holds vital clues about Earth's history. Sulfate-respiring bacteria and archaea in marine sediments favor ^{32}S over ^{34}S in their reduction of sulfate, yielding ^{34}S-depleted hydrogen sulfide; this signal can be traced back 2.5 to 2.7 billion years. Sulfate reducers only discriminate the isotopes at sulfate concentrations above ~1 millimolar. The isotope signal thus documents a sulfate-rich ocean (*2*).

The absence of this isotopic signal before 2.7 billion years ago (*3*) could mean that sulfate levels were low or that sulfate reduction had not yet evolved. In support of the former explanation, Shen *et al.* (*4*) have reported evidence that sulfate reducers existed 3.5 billion years ago. The authors found ^{34}S-depleted sulfide associated with a barium sulfate bed from North Pole, Western Australia.

The results of Shen *et al.* (*4*) are one of the two oldest reported datings of a specific energy metabolism. More recently, methanogenesis was dated to the same age (*5*). Carbon isotope analysis has provided evidence for biological carbon fixation by 3.8 billion years ago (*6*), but carbon fixation may be linked to different types of energy metabolism. Philippot *et al.* have now repeated the sulfur isotope analyses from North Pole with new samples, finding slightly more ^{34}S-depleted sulfide than the previous study. They also extended the analysis to ^{33}S, which gives information about the sulfur source. The results show that the simplest explanation is not always the right one.

For elements with several stable isotopes such as sulfur, isotopic fractionation in aqueous processes—including enzymatic ones—depends closely on the mass differences between the isotopes; for example, the fractionation between ^{33}S and ^{32}S is 0.515 times that between ^{34}S and ^{32}S (*7*). In contrast to this mass-dependent fractionation, atmospheric photochemical

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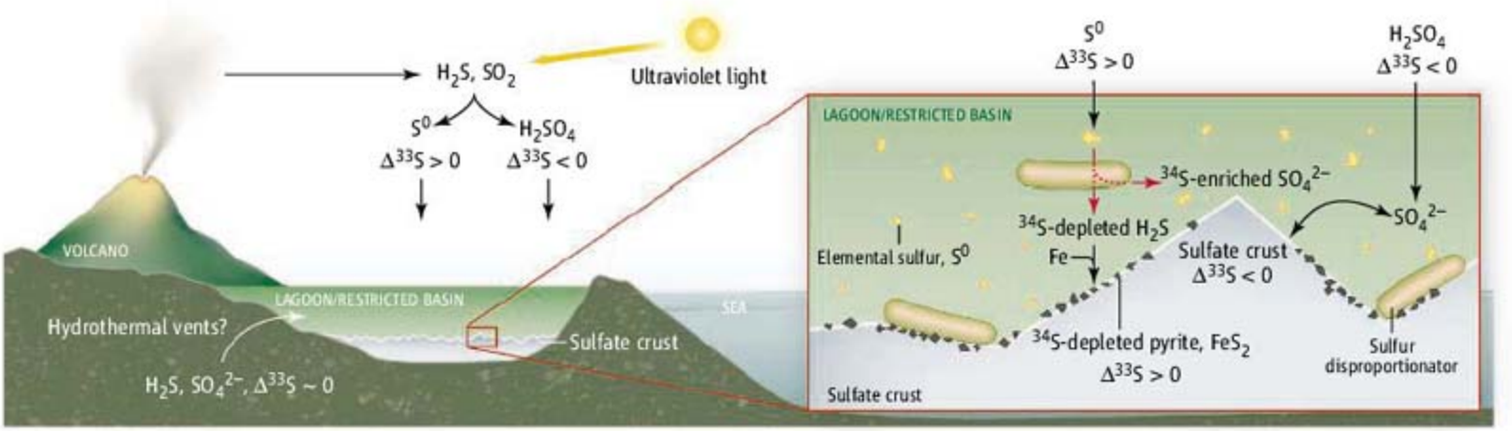

The sulfur cycle at North Pole according to (*1*). Atmospheric reactions of sulfur gasses induce a mass-independent fractionation with positive ^{33}S anomalies ($\Delta^{33}S$) in elemental sulfur (S^0) and negative anomalies in sulfuric acid (H_2SO_4). Sulfur and sulfate are deposited in a shallow, sulfate-rich basin. **(Inset)** Elemental sulfur is disproportionated by microbes, with mass-dependent fractionation into ^{34}S-depleted hydrogen sulfide and ^{34}S-enriched sulfate. Hydrogen sulfide precipitates as ^{34}S-depleted pyrite on the surface of the crust, whereas the sulfate is diluted into the large sulfate pool.

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reactions may result in mass-independent fractionation, seen as deviations from the fixed mass-dependent ratios.

Sulfur species from sediments older than 2.5 billion years exhibit large mass-independent fractionations, which are not found in younger sediments. This indicates that the early sulfur cycle was influenced strongly by atmospheric reactions (*7*). These reactions likely involved photolysis of volcanogenic H_2S and SO_2 by ultraviolet radiation, leading to the deposition of elemental sulfur with a positive ^{33}S anomaly and sulfate with a negative ^{33}S anomaly (see the figure) (*8*).

If the ^{34}S-depleted sulfur in pyrite from North Pole were produced by sulfate reduction, it should carry the same slightly negative ^{33}S anomaly as the sulfate from which it formed. Instead, the pyrite carries the positive ^{33}S anomaly predicted for atmospherically generated elemental sulfur. Only one known abiotic or biological elemental-sulfur transformation generates a substantial ^{34}S depletion at low temperature: the bacterial disproportionation reaction

$$4S^0 + 4H_2O \rightarrow 3H_2S + SO_4^{2-} + 2H^+.$$

Just three pure bacterial cultures that grow by sulfur disproportionation are known (*9*, *10*). These bacteria are the masters of simple inorganic life. For example, *Desulfocapsa sulfoexigens* needs only water, sulfur, CO_2, and inorganic nutrients for growth (*9*). It obtains energy from the hydrolysis of elemental sulfur, thiosulfate, or sulfite and grows anaerobically as long as the concentration of H_2S produced is kept low (*11*).

The strict environmental requirements of known sulfur-disproportionating bacteria—an anoxic environment colder than ~40°C with near neutral pH and low hydrogen sulfide concentrations (*9*)—may help to clarify divergent interpretations of the North Pole paleoenvironment (*12*, *13*). However, caution is needed with such conjectures: This group of bacteria has received so little attention that other species with different environmental preferences may have escaped the microbiologists' notice.

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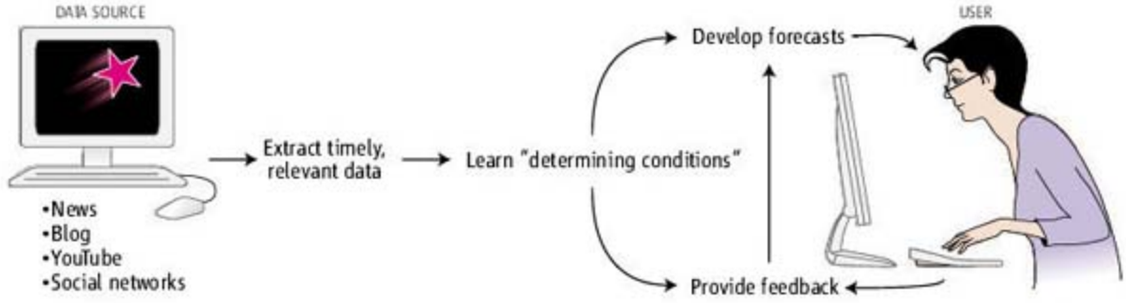
COMPUTER SCIENCE

Cultural Modeling in Real Time

Computer models are being developed that can help policy-makers predict the behavior of political, economic, and social groups.

V. S. Subrahmanian

Several recent examples show the difficulties governments and organizations have in predicting the consequences of their actions. In 2001, U.S. commanders were unable to successfully negotiate deals with local tribesmen to prevent the escape of bin Laden, even though reports indicate that they had excellent intelligence on where he was. The day after the United Nations approved a resolution calling for the deployment of 17,300 peacekeepers to Sudan, the Sudanese government launched a major offensive in Darfur. In December 2006, an unexpectedly large group of protesters in Kyrgyzstan marched against the decision by their government to enter a debt-relief program under the auspices of the World Bank.



Building a real-time sociocultural model. Data gathered from many sources is sifted for relevant information. Modeling software takes this information to extract "determinant conditions" or situations that could lead to possible actions of members of a group. The models can forecast future actions and refine those forecasts with feedback from users.

Accurate forecasts depend critically upon the ability to build behavioral models of the people and groups involved. Social scientists have traditionally constructed cross-cultural models by conducting either in-person or written surveys (*1*), or living with such groups (*2*), and then hypothesizing and testing correlations in collected data by means of various statistical models (*3*). None of these strategies will work in countries riddled with conflict like Iraq and Sudan today. Old surveys are likely to be outdated. Questionnaires and survey respondents may be influenced by the climate under which the survey is taken. In conflict situations, data must be gathered with real-time methods. However, building behavioral models in real time is particularly difficult (see the figure).

Computational social models may offer the best solution in cases where conventional data gathering is not possible. Tools such as The Resource Description Framework Extractor (T-REX) (*4*) use socio-cultural-political-economic-religious (SCPER) variables provided by social scientists in conjunction with other data sources (e.g., surveys), if available, and automatically extract relevant data from news sources, blogs, newsgroups, and wikis (i.e., collaboratively written information sharing sites). Other efforts such as the KEDS project (*5*) extract variables from specific news sources. The SCPER variables can include financial activities, violent event information, or political relationships. The source data can be automatically analyzed to

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recognize spikes in such activities, providing "early warnings" of potential conflicts. Unlike past methods, these methods do not require previous knowledge of the groups being investigated.

Past behavioral models [e.g., to forecast turmoil in Indonesia (*6*)] were painstakingly built by hand. Building behavioral models in real-time from such data is a challenge that is only now being addressed by software development.

Systems such as the Cultural Reasoning Architecture (CARA) (*4*) can be used to study the Janjaweed in Sudan (a militia of Arab descent engaged in the systematic use of mass rape and violent attacks against Muslims of non-Arab descent in the Darfur region). Data may include parameters that indicate increases or decreases in these actions. In another example, the probability of suicide attacks by the Lebanese Shiite group Hezbollah when they are not engaged in rocket attacks and car bombings depends upon whether Hezbollah was using education and propaganda as a major part of their strategy. When they were, the probability of suicide attacks was around 47%, but when they were not, the probability shot up to 80%. This is one example of a rule automatically discovered by the CARA architecture (*4*) with the "Minorities at Risk" data set (*7*). The number of possible determining conditions is enormous, and a human analyst could easily miss an interesting hypothesis. Moreover, because programs like T-REX provide a flood of data (45,000 pages per day), sophisticated algorithms are needed. Classification algorithms (*8*) to identify conditions that neatly separate desirable situations from undesirable ones (e.g., violent actions versus more acceptable forms of negotiation) offer an excellent starting point, although substantial scaling to huge data sets is required.

We can use these methods to model terror groups, political parties, U.S. allies, companies, or regulatory bodies. The final step is to forecast how members of the modeled group may act once a set of determining conditions has been found. Even if we study just 1000 actions, there are 2^{1000} possible sets of actions that a group might take at just the next time point. This corresponds to about 10^{300} possible sets of actions. Current systems such as the stochastic modeling agents in the CARA (*4*) architecture can estimate the k most probable sets of action the opponent might take in a few minutes when 10^{27} sets of actions are involved. The ability to access real-time information on these topics, to rapidly analyze the possible actions that interested parties might engage in, and to determine how best (e.g., with methods of game theory) to respond, will provide a key tactical advantage to organizations that are entering foreign cultures with goals as diverse as stopping terrorism or improving corporate profits.

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MICROBIOLOGY

Sizing Up the Uncultivated Majority

A new imaging technique allows the metabolic activity of single microbial cells to be quantified in environmental samples.

Marcel M. M. Kuypers

Coupling the identity of microbes with their activity in the environment remains an important gap in our ability to explore microbial ecology. The development of techniques to quantify the metabolic activity of single microbial cells has been especially challenging, mostly due to their small size. Microbiologists are therefore excited about a new high-resolution imaging method called multi-isotope imaging mass spectrometry (MIMS) or nanoSIMS, which can help decipher what individual microbes are "doing" in the environment. On page 1563 of this issue (*1*), Lechene and colleagues apply MIMS to identify a symbiotic relationship between a nitrogen-fixing bacterium and an animal host. The technique is poised to reveal the metabolic diversity of the planet's microorganisms, 99% of which has eluded cultivation (*2*).

MIMS can determine the chemical, radioisotopic, and stable-isotopic composition of biological material down to the submicrometer level (*3*–*6*). By exposing microbial communities to substrates that have been labeled with stable isotopes, MIMS-based imaging allows visualization of metabolic activity in single cells. Moreover, nutrient uptake rates and fluxes can be quantified.

Lechene *et al.* used MIMS to quantify nitrogen (N_2) fixation by individual bacteria that inhabit the gills of the shipworm *Lyrodus pedicellatus*. *L. pedicellatus* is a wood-eating marine bivalve with little nitrogen in its diet and must therefore rely on other nitrogen sources (*7*). Previous studies reported N_2 fixation for intact shipworms, as well as for pure cultures of bacterial symbionts isolated from shipworm gills (*7*, *8*), but neither the site of fixation nor whether the fixed nitrogen is supplied to the host could be determined. Lechene *et al.* grew shipworms in seawater containing nitrogen gas enriched in the rare stable isotope ^{15}N and used MIMS to measure ^{15}N incorporation in symbionts and shipworm tissue (see the figure). The incorporation of ^{15}N was determined by comparing the quantitative mass images of $^{12}C^{14}N^-$ and $^{12}C^{15}N^-$—produced by bombardment of tissue with a cesium ion beam—to measure the increase in $^{15}N/^{14}N$ ratios relative to the natural abundance ratio (0.00367). Transmission electron microscopy of the same shipworm gill tissue was used to identify bacteria and host cells. The combined data provide the first direct evidence for in situ N_2 fixation by bacterial symbionts and demonstrate that this nitrogen is used by the shipworm host.

Until the work of Lechene *et al.*, it had not been possible to quantify the incorporation of nitrogen by individual N_2-fixing microorganisms or to map the fate of fixed nitrogen in the microbial environment. Other methods currently used either do not provide single-cell

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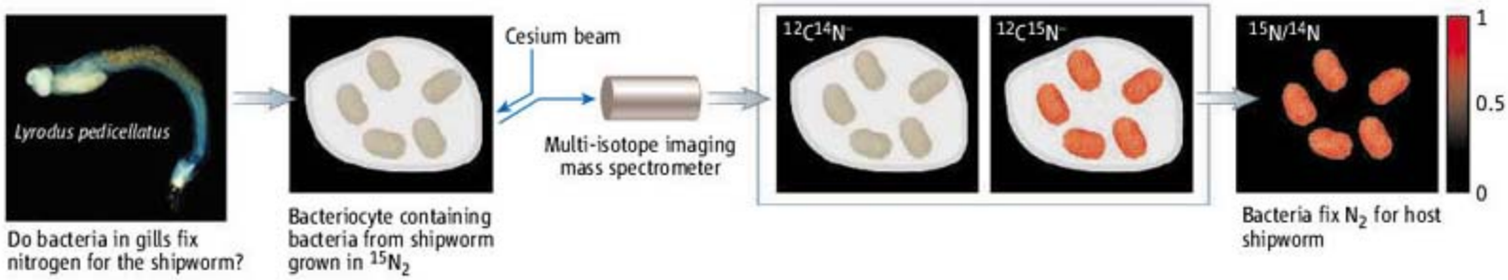

A new window on microbial activity. The incorporation of ^{15}N stable isotope into a mixed population of cells (animal cells and bacteria) is determined by comparing two quantitative mass images ($^{12}C^{14}N^-$ and $^{12}C^{15}N^-$) obtained by multi-isotope imaging mass spectrometry (MIMS). The increase in $^{15}N/^{14}N$ ratios relative to the natural abundance ratio can then be measured to identify the fate of the ^{15}N.

resolution or, like micro-autoradiography, require that microorganisms be fed radioactive-labeled substrates (*9*). The uptake of radiolabeled isotopes directly links individual microbial cells to their activity in the environment. However, because this approach requires radioactivity, its use is limited to elements that have a radioisotope with a suitable half-life (>1 day; for example, ^{14}C and ^{3}H) and excludes the study of other elements such as nitrogen. MIMS, on the other hand, can be used to measure the distribution of any stable isotope as well as any radioisotope with a suitable half-life. Hence, the approach used by Lechene *et al.* holds great promise for studying symbiont-host interactions and microbial activity in the environment.

Combining MIMS with fluorescence in situ hybridization (FISH) is an even more powerful technique for identifying and characterizing single microbial cells. FISH uses fluorescent-labeled probes that are specific to the organism of interest and that bind to the intracellular 16*S* ribosomal RNA (*2*). Replacing fluorescent probes with isotopically labeled (stable or radioactive) or halogenated probes would allow individual cells to be directly identified (by probe hybridization to targets) by MIMS (*10*). The hybridization procedure is essentially identical to that used for FISH, and the same probes can be applied. By combining this probing technique with isotope labeling of substrate, one can assess the metabolic activity of cells and simultaneously identify their phylogenetic characteristics during a single MIMS scan. This approach links the identity of microbial cells to their in situ activity. MIMS is truly an imaging breakthrough, whose application is only just beginning to yield information once considered inaccessible.

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ASTRONOMY

From Darkness to Light

A supercomputer simulation shows that matter in the early universe might have formed dense filaments before collapsing into the first stars.

Volker Bromm

What is the nature of the dark matter that is believed to dominate the structure of the universe at large scales? How did the cosmic dark ages end when the first stars lit up the universe again a few hundred million years after the Big Bang? These questions might be intimately related. On page 1527 of this issue, Gao and Theuns (*1*) present numerical simulations of cosmological structure formation in the early universe. Their simulations demonstrate how sensitively the formation of the first stars depended on the detailed properties of the still mysterious dark matter. The macrophysics of early star formation might thus hold important lessons for the microphysics of exotic elementary particles.

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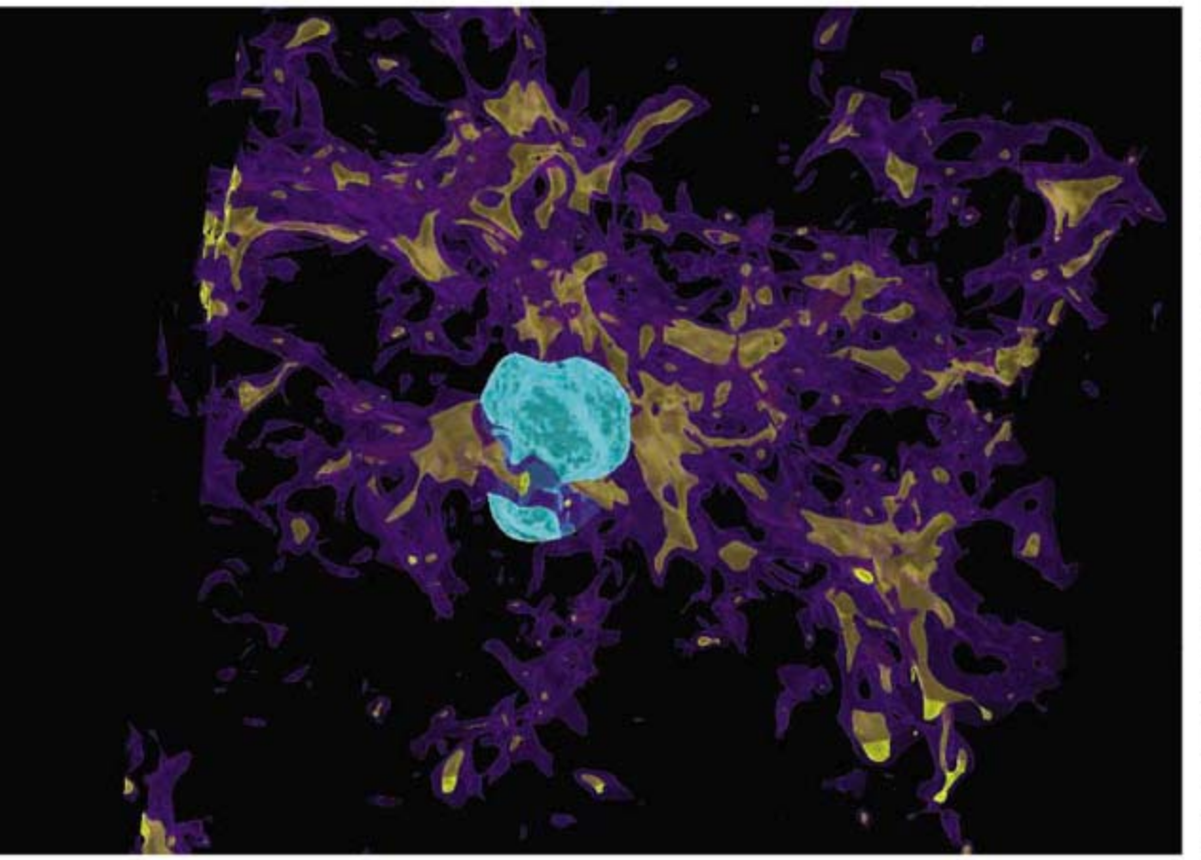
According to the standard model (*2*), star formation in the early universe was very different from the present. Stars today form in giant clouds of molecular gas and dust embedded in the disks of large galaxies like our Milky Way, whereas the first stars emerged inside "minihalos," agglomerates of primordial gas and dark matter with a total mass of a million times that of the Sun.

Another difference arises from the initial absence of elements other than the hydrogen and helium that were synthesized in the Big Bang. Gas clouds today can efficiently cool via radiation emitted by atoms, molecules, or dust grains that contain heavy elements. Because the primordial gas lacked those coolants, it remained comparatively hot. For gravity to overwhelm the higher thermal pressure, the mass of the first stars must have been larger as well. Numerical simulations have led most researchers to believe that the first stars were predominantly very massive, typically a few hundred solar masses.

The emergence of the first stars fundamentally changed the early universe at the end of the cosmic dark ages (*3*). Owing to their high mass, these stars were copious producers of heavy chemical elements that were rapidly dispersed by supernova explosions. They also produced many ultraviolet photons that were energetic enough to ionize hydrogen, the most abundant element in the universe. Thus began the extended process of what cosmologists call "reionization" (see the figure), which transformed the universe from a completely cold and dark neutral state into the fully ionized medium of today. Observations of the polarization in the cosmic microwave background (CMB), due to the scattering of CMB photons off free electrons, place constraints



Cosmic renaissance. This supercomputer simulation shows a primordial star of 100 solar masses, formed inside a dark matter minihalo and surrounded by a bubble of ionizing radiation (light blue). The bubble is embedded in the still-neutral cosmic gas (weblike structure in shades of purple and yellow). This frame depicts the initial step in the process of cosmic reionization.

on the onset of reionization. Measurements made with the Wilkinson Microwave Anisotropy Probe (WMAP) indicate that about 10% of the total signal was likely produced by the first stars (*4*).

Our picture of how the first stars formed and how they affected the evolution of the cosmos assumes that dark matter is made up of weakly interacting massive particles (WIMPs). Such particles are predicted by several theories but are as yet undetected because they interact with normal matter only via gravity and the weak nuclear interaction. A plausible WIMP candidate is the "neutralino," the lightest "superpartner" in many supersymmetrical theories (*5*). Supersymmetry postulates that for every known particle there is a superpartner, thus effectively doubling the zoo of elementary particles. Most of these superparticles that were produced briefly after the Big Bang are unstable and have decayed. The lightest of them, however, could not decay into any other particle and thus would exist today.

The neutralino is expected to be rather massive, having roughly the mass of a hundred protons, and so it would move comparatively slowly (it would be "cold"). Such cold dark matter (CDM) particles preserve any density perturbations from the very early universe. To see this, consider the opposite case in which the dark matter would be "hot," corresponding to very light particles. Streaming velocities would then be very large, and such hot dark matter could not be trapped in small density condensations. The first structures to form in the universe would then be large, massive systems, whereas in CDM models, small-scale structures would survive and would be the first to emerge.

CDM models predict that the first stars formed in dark matter minihalos. In turn, the evolution of the primordial gas falling into these minihalos yields stars with roughly a hundred times the mass of the Sun. Gao and Theuns are now challenging this CDM-based standard view. They consider a situation in which the dark matter is slightly less cold, termed "warm dark matter" (WDM). WDM models agree with CDM models on large scales, but they lead to drastically different predictions for the small scales that are relevant for the formation of the first stars. In the WDM scenario investigated by Gao and Theuns, there are no minihalos that could host the formation of the first stars; instead, the primordial gas would collapse first into massive filamentary structures. The completely different history experienced by the star-forming gas would likely result in stars with a different distribution of masses, possibly skewed toward somewhat less massive stars. The simulations presented here cannot yet resolve the formation of the actual stars, rendering any conclusions about the precise stellar masses tentative.

How do we decide between the CDM and WDM models? One way is to compare the predicted strength of the CMB polarization signal with the WMAP measurement (*6*). If the suppression of small-scale features in WDM models is too severe to produce enough ionizing photons, such scenarios can be excluded. A complementary strategy to empirically probe the mass and mass distribution of the first stars is to hunt locally for fossils of the dark ages, low-mass stars in our Milky Way that contain only a tiny amount of heavy elements. These would carry the imprint of the first stars that produced those elements with an abundance pattern that sensitively depends on mass (*7*, *8*). Again, the simulations are not yet detailed enough to make predictions with the required degree of precision, but the game is clearly on now.

This new frontier of connections between particle physics and the first stars offers intriguing possibilities. If dark matter particles could decay, or if they were concentrated so that annihilation reactions could occur, then heating of the primordial gas would result, with the potential to greatly modify star formation (*9*, *10*). Cosmology has a huge stake in the search for possible dark matter candidates soon to be carried out at the Large Hadron Collider at CERN.

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Complexity of Coupled Human and Natural Systems

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Integrated studies of coupled human and natural systems reveal new and complex patterns and processes not evident when studied by social or natural scientists separately. Synthesis of six case studies from around the world shows that couplings between human and natural systems vary across space, time, and organizational units. They also exhibit nonlinear dynamics with thresholds, reciprocal feedback loops, time lags, resilience, heterogeneity, and surprises. Furthermore, past couplings have legacy effects on present conditions and future possibilities.

Coupled human and natural systems are integrated systems in which people interact with natural components. Although many studies have examined human-nature interactions (*1*–*5*), the complexity of coupled systems has not been well understood (*6*, *7*). The lack of progress is largely due to the traditional separation of ecological and social sciences (*8*). Although some scholars have studied coupled systems as complex adaptive systems (*9*, *10*), most of the previous work has been theoretical rather than empirical.

An increasing number of interdisciplinary programs have been integrating ecological and social sciences to study coupled human and natural systems (e.g., social-ecological systems and human-environment systems). Here, we synthesize six case studies to demonstrate the approaches used and results found (Fig. 1 and table S1). These studies are on five continents: the Kenyan Highlands in Africa (Kenya); the Wolong Nature Reserve for giant pandas in China (Wolong); Central Puget Sound of Washington (Puget Sound) and Northern Highland Lake District of Wisconsin (Wisconsin) in the United States; an area near Altamira, State of Pará, Brazil (Altamira); and Kristianstads Vattenrike of Sweden (Vattenriket) (Fig. 1). They include urban (Puget Sound), semi-urban (Vattenriket), and rural areas (Altamira, Kenya, Wisconsin, and Wolong), and they are in developed countries (Puget Sound, Wisconsin, and Vattenriket) and developing countries (Altamira, Kenya, and Wolong). These studies are in different ecological, socioeconomic, political, demographic, and cultural settings, and they encompass a variety of ecosystem services and environmental problems (table S1).

These studies share four major features. First, they explicitly address complex interactions and feedback between human and natural systems. Unlike traditional ecological research that often excluded human impacts or social research that generally ignored ecological effects, these studies consider both ecological and human components as well as their connections. Thus, they measure not only ecological variables (e.g., landscape patterns, wildlife habitat, and biodiversity) and human variables (e.g., socioeconomic processes, social networks, agents, and structures of multilevel governance) (*11*), but also variables that link natural and human components (e.g., fuelwood collection and use of ecosystem services). Second, each study team is interdisciplinary, engaging both ecological and social scientists around common questions. Third, these studies integrate various tools and techniques from ecological and social sciences as well as other disciplines such as remote sensing and geographic information sciences for data collection, management, analysis, modeling, and integration (*11*–*15*) (table S1). Fourth, they are simultaneously context-specific and longitudinal over periods of time long enough to elucidate temporal dynamics. As such, these studies have offered unique interdisciplinary insights into complexities that cannot be gained from ecological or social research alone.

Reciprocal Effects and Feedback Loops

In coupled human and natural systems, people and nature interact reciprocally and form complex feedback loops. For example, local residents in Wolong use forests as fuelwood for cooking and heating. As forests near households were depleted due to fuelwood collection (*16*), local residents had to collect fuelwood from areas far away (*17*). Because these forests are bamboo forests (habitat for the endangered giant panda) and the bamboo in the forests is the staple food for the panda, fuelwood collection has led to substantial deterioration in forests and panda habitat (*16*). To prevent further degradation and restore panda habitat, the Chinese government began to implement three major conservation policies several years ago, which help both local residents and panda habitat. In Kenya, local residents convert forests into cropland and intensively cultivate land without supplying additional nutrients, in some cases for more than 100 years. Soil degradation with the resulting decreases in crop yields and greater food insecurity hastens conversion of remaining forests to agriculture. Similarly, in Altamira, 255,739 hectares (ha) of forests had been converted into pasture and cropland as of 2003. As soil quality declines, fertilizers must be applied, crops are shifted to those with lower nutrient requirements, or more forests are converted into cropland (there were still 136,913 ha of forested area in 2003).

Feedback between human and natural systems in the agricultural and tourism sectors of developed countries is in many ways similar to feedback in developing countries. For example, local people (76,000 in 2005) in Vattenriket benefit from ecosystem services that are the result of long-term human management of the agricultural landscape. In Wisconsin, ecosystem conditions affect tourism, which is the mainstay of the economy, but economic development and ecosystem exploitation from tourism often degrade the qualities that attract tourists.

The ecological and socioeconomic patterns and processes in urban coupled systems are different from those in rural areas. They are mediated by factors such as the urban form, built infrastructure, and location and consumption preferences of heterogeneous households and businesses. For example, in Puget Sound, a distinctive spatial heterogeneity can be observed across an urban to rural gradient in relation to diverse development patterns (*18*). Land-cover changes influence biophysical processes (e.g., water purification) and stream biotic integrity (*15*). Furthermore, changes in land cover due to development in turn affect land value and real estate markets, as evidenced by values of real estate having up to a 6.5% premium associated with forest cover (*19*).

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Dynamics of human-nature systems are influenced by many factors, including government policies and contextual factors in which local processes are shaped by larger-scale and ultimately global-scale processes (*20*). Both markets and governance can cause decisions made in one place to affect people and ecosystems far away. For instance, economic opportunities in cities attracted many local residents from Wolong to work in cities in the past several years, thus reducing fuelwood collection and consumption. Compared with the migrant workers in cities from Wolong, however, more than a thousand times more tourists from around the world increased the demand for fuelwood through consuming local products, whose production may require fuelwood and electricity.

Nonlinearity and Thresholds

Numerous relationships in coupled systems are nonlinear. In Wisconsin, for instance, fallen trees that provide critical fish habitat in lakes and streams drastically decrease when housing density exceeds about seven houses per kilometer of shoreline (Fig. 2). Bird richness in the Puget Sound landscape with single-family housing and fragments of native forest increases nonlinearly with forest cover and peaks when 50 to 60% of the land is forested (Fig. 3) (*21*).

Thresholds [transition points between alternate states (*22*)] are common forms of nonlinearity. In Vattenriket, an intentional participatory process mobilized stakeholders laying the groundwork for a shift from conventional management to adaptive co-management (*23*). Cultural values and environmental concerns prompted local stakeholders to build new knowledge, develop new visions and goals, and create new social networks. The result of these community activities was a new and more suitable governance system of adaptive co-management of the landscape.

System behaviors shift from one state to another over time (temporal thresholds) and across space (spatial thresholds). Altamira depicts a temporal threshold, whereas Wolong demonstrates a spatial threshold. Deforestation rates in Altamira are high during the first 5 to 7 years of settlement and then decrease rapidly. In Wolong, as the distance between locations of households and fuelwood collection sites increases, panda habitat decreases, reaching a minimum at a distance of approximately 1800 m (*17*). When the distance between households and fuelwood supplies is small, the total area for fuelwood collection is small and thus panda habitat is better protected. When the distance is large (>1800 m), fuelwood collection is scattered throughout a large region and affected areas can recover relatively quickly. When the distance is approximately 1800 m, local residents' fuelwood demand is met by cutting most available trees and causes more habitat loss (*17*).

Surprises

When complexity is not understood, people may be surprised at the outcomes of human-nature couplings. For example, smelt (*Osmerus mordax*) was initially introduced to Wisconsin as a prey species for game fish such as walleyes (*Stizostedion vitreum*), but smelt ate juvenile walleyes leading to loss of walleye populations. In Puget Sound, growth management policy has caused urban density to intensify inside the urban growth boundary while unintentionally facilitating sprawl outside the urban growth boundary.

Conservation policies can also generate unintended perverse results. In Wolong, for instance, high-quality panda habitat degraded faster after the area was established as a reserve than before the reserve's creation (*24*). To prevent

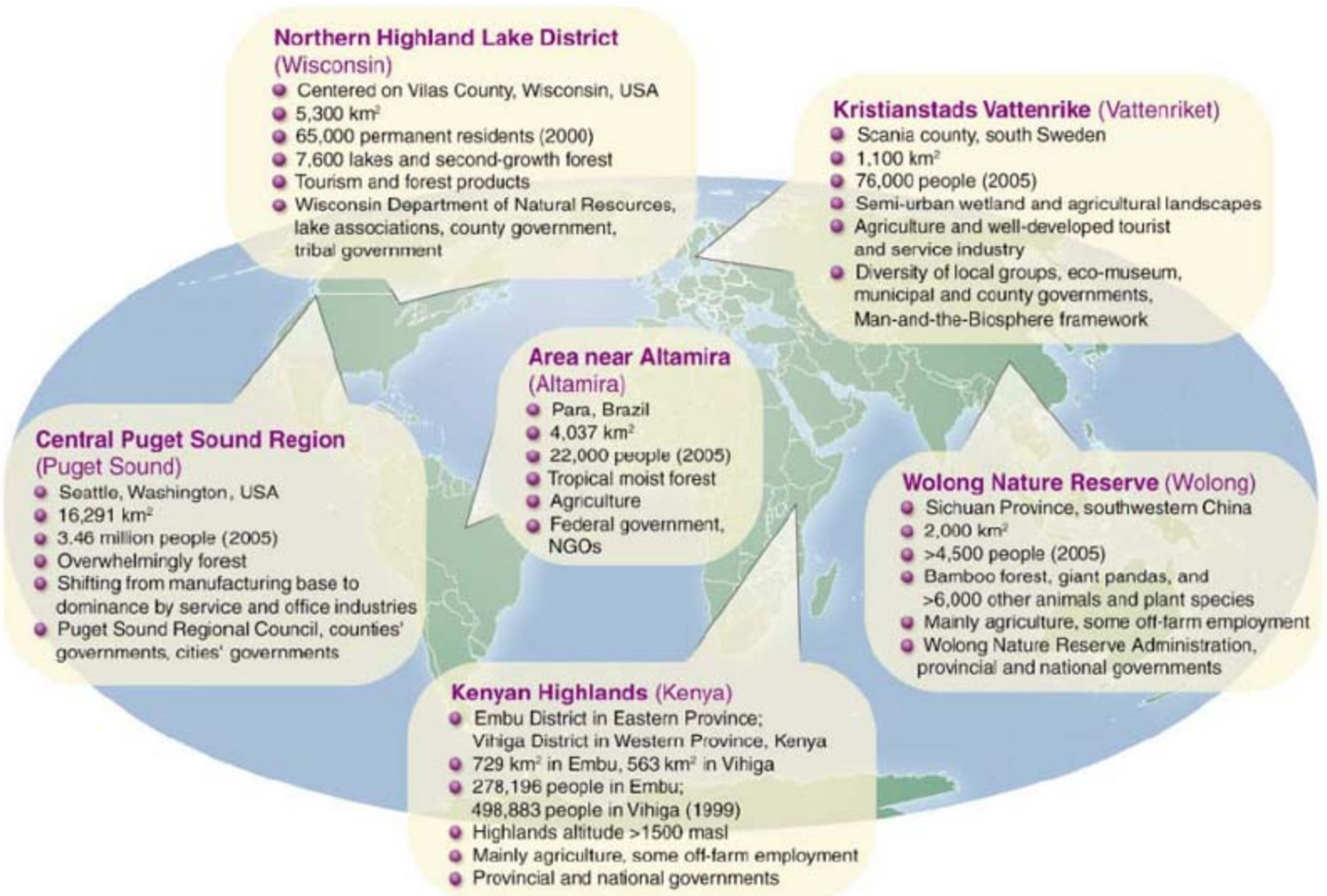

Fig. 1. Map highlighting major attributes of the six coupled human and natural systems (location; spatial extent; population size; and ecological, economic, and administrative attributes). To save space, short names within the parentheses represent the coupled systems. See table S1 for more detailed descriptions.

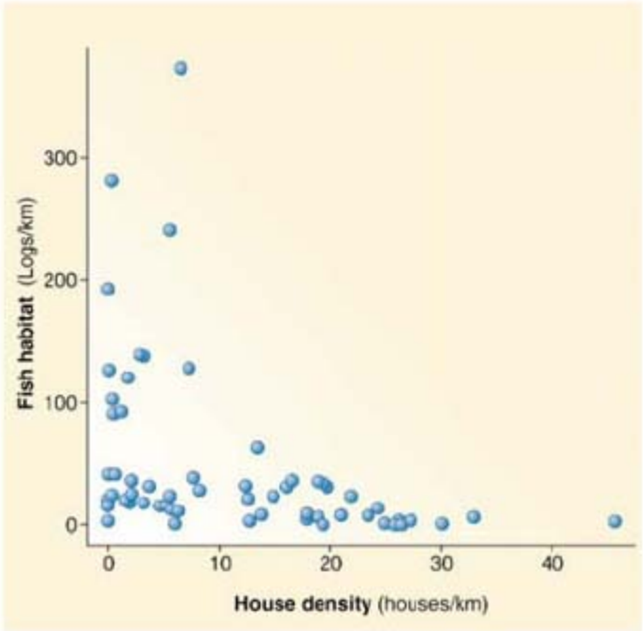

Fig. 2. The relationship between fish habitat (logs per kilometer) and house density in the Northern Highland Lake District of Wisconsin, United States. [modified from (*38*), with permission]

further degradation, a natural forest conservation program was introduced in 2001 for local residents to monitor illegal harvesting. Unexpectedly, a large number of new households formed in 2001 because many households decided to split into smaller ones to more effectively capture subsidies (20 to 25% of the average household income) given to households as part of the program. The household proliferation and reduction in household size (number of people in a household) increased demand for fuelwood and land for house construction (*25*).

Some ecosystems can only be sustained through human management practices, whereas many conservation efforts preclude such human interference. For example, the wetland site under the Ramsar Convention (an international treaty for the conservation and sustainable use of wetlands) in Vattenriket was set aside for conservation purposes, but the wetland became overgrown when grazing was halted. This unintended consequence led to an understanding of grazing as essential to maintaining this wetland system (*23*).

Legacy Effects and Time Lags

Legacy effects are impacts of prior human-nature couplings on later conditions. Among the six sites, legacies vary in duration from decades to centuries. The shortest legacy is in Altamira, a frontier area where the land tenure system imposed by the government in 1970 still shapes the present spatial pattern of land-cover change, human population distribution, and human activities. The longest legacy is in Vattenriket, where the landscape has been affected by human actions such as using wet grasslands over hundreds of years.

Legacy durations in the other sites fall somewhere in between. In Wolong, current forest types in areas at lower elevations (1200 to 3000 m) are shaped by forest harvesting three to nine decades ago. Introduction of a keystone species can restructure a fish population for decades or longer, as has been demonstrated in the Wisconsin study area which started fish stocking in the 1930s. Long-term (up to 100 years) continuous cultivation in Kenya has decreased crop yields, with most of the degradation occurring during the first 15 to 20 years after conversion from forest to agriculture. In Puget Sound, landscape patterns are influenced by infrastructure built decades or even a century ago.

The ecological and socioeconomic impacts of human-nature couplings may not be immediately observable or predictable because of time lags between the human-nature interactions and the appearance of ecological and socioeconomic consequences. In Kenya, there is a time delay between investment in soil improvement and increases in income. In Vattenriket, the city of Kristianstad stopped taking its drinking water from the Helgeå River in the 1940s because untreated industrial and household sewage had accumulated several decades earlier. Disturbances to groundwater quality can take a long time to appear "downstream" because groundwater movement between adjacent lakes can take centuries. In Puget Sound, ecological effects of the Growth Management Act adopted in the State of Washington in 1990 could not have been observed in less than 8 years (*26*).

The length of lags attributable to a single cause may vary for different indicators; conversely, different causes may become apparent over different time periods for the same indicator. The former can be seen in Altamira, where changes in crop prices quickly affect planting of annuals but effects on planting (or abandonment) of perennials (such as cocoa and black pepper) often are delayed. As to the latter situation, changes in the price of electricity quickly affect panda habitat in Wolong because of sharp changes in fuelwood demand, but spacing of births within households has a much slower effect (*27*). Energy for cooking is needed daily and fluctuations in the price for electricity may quickly force local residents to use more fuelwood (thus destroying forests and panda habitat), whereas it takes a longer time for children to establish new households that increase demand for energy.

Resilience

Coupled systems have different degrees of resilience—the capability to retain similar structures and functioning after disturbances for continuous development (*10*, *28*, *29*). Resilience can be affected by many factors. In Wolong, for example, larger areas with fast-growing tree species are more resilient to fuelwood collection than are smaller areas with slower-growing trees. In Kenya, remittances from relatives employed in urban areas minimize food insecurity due to crop failures caused by droughts and poor soil fertility.

Human intervention also plays a key role in maintaining resilience. For instance, in Vattenriket, sustaining the resilience of the wetland landscape requires grazing by cattle and incentives to make grazing economically viable. Partially because of the actions of environmentalists, Puget Sound is still home to one of the last intact old-growth forests in the United States despite rapid urbanization. In Wisconsin, social-ecological resilience comes from the good condition of many ecosystems; the intention of Native Americans to manage their lands and lakes sustainably; the mosaic of tribal, private, and state ownership; and innovations in ecosystem management by various stakeholders (tribal governments of Native Americans, lake associations, formal research organizations, and nongovernment organizations) (*12*).

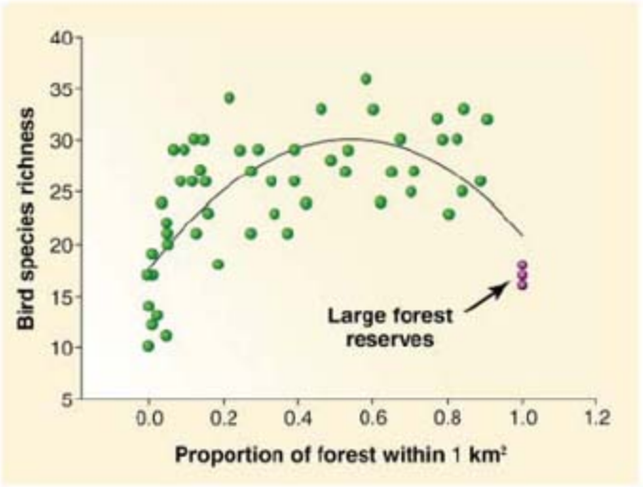

Fig. 3. Change in avian richness with progressively more forest (less human settlement) in the human-influenced landscape in Central Puget Sound region of Washington, United States. [modified from (*21*), with permission]

Heterogeneity

Human-nature couplings vary across space, time, and organizational units. The socioeconomic differences among people in Wisconsin lead to different choices and behaviors, which in turn result in very different ecological outcomes than

one would find were everyone to have the same preferences for ecosystem services. In Altamira, different settlement cohorts follow similar trajectories of land use, but the magnitude of changes in important variables like rates of deforestation varies as a product of exogenous and endogenous factors (e.g., local, regional, and global political economy) (*30*). For the Kenyan highlands, it is common to find families with soils of different quality and as a result, different crop yields.

Coupled human-natural systems are not static; they change over time. Although the human population sizes have increased in all six study sites over the past several decades, the resultant ecological impacts have differed. In the Kenya study area, human population size has doubled over the past 30 years, causing a marked reduction in farm size. Smaller farm size has led to growing maize during both rainy seasons to meet family demand, but this practice has accelerated the rate of soil degradation and increased poverty. An increase in recreational land use in Wisconsin led to a 4.6-fold increase in housing density (from 3.7 to 17.2 units/km^2) from 1940 to 2000. For Puget Sound, between 1991 and 1999 land area covered by development increased by 620 km^2 (31.5% increase), while forest cover declined by 714 km^2 [10.3% decline (*26*)]. Temporal changes take place not only inside a coupled system, but also across its boundaries. In Wolong, a rapidly increasing number of domestic and foreign tourists have made the system much more tightly coupled to the national and global economy.

Spatial variations exist in all coupled systems. For example, more fuelwood is collected in areas of Wolong with easy access and little enforcement than in forested areas with more challenging topography or strict enforcement. In Vattenriket, habitats and management practices, local stewardship associations, social networks, and multilevel institutions vary across the landscape (*11*). Landscape heterogeneity of Puget Sound increases with the degree of urbanization, but differs substantially within the region depending on urban land-use patterns, infrastructure, and spatial distribution of activities (*18*). In Wisconsin, people have preferentially settled around lower-elevation lakes, which tend to have riverine inputs, low to moderate dissolved organic carbon, low to moderate nutrients, and relatively diverse sport fish communities (*31*). In Altamira, fertile soils permit cultivation of cocoa and sugar cane, whereas on poorer soils, pasture and manioc cultivation are more common.

Conclusion and Outlook

Results such as those reviewed here benefit from and help advance the integration of ecological and social sciences. The approaches used and the results from these studies can be applied to many other coupled systems at local, national, and global levels. For instance, the finding that the number of households increased faster than the human population size in Wolong over the past three decades has led to the discovery that this trend is global and is particularly profound in the 76 countries with biodiversity hotspots (*25*). The Lake Futures Project (*32*) in Wisconsin was a prototype used to develop approaches for the Millennium Ecosystem Assessment scenarios (*33*).

Comparison of these studies provides important insights into diverse complex characteristics that cannot be observed in a single study. The types of surprises found in the case studies differ, although all of them originated from the interactions between human and natural systems. All six studies have demonstrated legacy effects, but legacy durations varied from decades to centuries. Because of the independent nature of these studies, information from one study is not necessarily available in or transferable to other studies. To increase the extent of generalizing from case studies, future research on coupled systems must include not only separate site-specific studies but also coordinated, long-term comparative projects across multiple sites to capture a full spectrum of variations (*14*, *34*, *35*). Furthermore, all the studies in this review focus on interactions within the system, rather than interactions among different coupled systems. As globalization intensifies, there are more interactions among even geographically distant systems and across scales (*36*, *37*). Thus, it is critical to move beyond the existing approaches for studying coupled systems, to develop more comprehensive portfolios, and to build an international network for interdisciplinary research spanning local, regional, national, and global levels.

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Supporting Online Material

www.sciencemag.org/cgi/content/full/317/5844/1513/DC1
Table S1

10.1126/science.1144004

Production of Trout Offspring from Triploid Salmon Parents

Tomoyuki Okutsu,[1] Shinya Shikina,[1] Megumi Kanno,[1] Yutaka Takeuchi,[1] Goro Yoshizaki[1,2]*

In recent decades, the number of salmonid species has declined markedly, and several species have become extinct or endangered. Because cryopreservation of fish eggs is difficult due to their large size and high fat content, we investigated the potential of surrogate broodstock technologies as a new method of genetic resource preservation for fish. Surrogate broodstock technologies involve the transplantation of primordial germ cells (PGCs) (*1*) or spermatogonia (*2*) from a target fish species into a related species for which rearing techniques are well developed. In doing so, the recipient species can produce sperm and eggs of the target species (*3*). Furthermore, because PGCs and spermatogonia are sufficiently small for cryopreservation, animals can be generated via the transplantation of thawed PGCs or spermatogonia into recipients, even if the target species becomes extinct. In prior work, we demonstrated that most spermatozoa produced by xenogeneic recipients are of recipient origin; few donor-derived spermatozoa are produced (*4*). In addition, the production of viable donor-derived eggs in xenogeneic recipients has not yet been observed in any animal species to date. The present study therefore attempted to produce only donor-derived sperm and eggs by transplanting spermatogonia into sterile xenogeneic recipients.

In this study, spermatogonia of p*vasa-Gfp* (where Gfp represents green fluorescent protein) hemizygous (p*vasa-Gfp*/–) and dominant orange-colored mutant heterozygous [*OR*/*wild type* (*WT*)] adult rainbow trout (*Oncorhynchus mykiss*) were intraperitoneally microinjected into newly hatched embryos of triploid sterile masu salmon (*O. masou*). Hybrids of these two species do not survive. Histological examination showed that, whereas the testes of 2-year-old triploid salmon in the control group (no transplantation) were immature and contained mostly spermatogonia, testes of recipients appeared normal (Fig. 1A). Ten of the 29 male triploid salmon recipients produced milt. Offspring produced with milt from these 10 recipients and wild-type trout eggs developed normally (fig. S1 and table S1). Five F_1 progeny were collected from each of the 10 recipients (n = 50) for species determination using random amplified polymorphic DNA (RAPD) analysis. All 50 specimens exhibited the same DNA fingerprint patterns as rainbow trout (fig. S2), indicating that male triploid salmon recipients produced only donor-derived trout.

The ovaries of four of the eight female recipients contained vitellogenic oocytes at 17 months post transplantation (Fig. 1B). All vitellogenic oocytes exhibited donor-specific green fluorescence. Ovaries of intact triploid salmon of the same age contained no vitellogenic oocytes (Fig. 1B). When recipients reached 2 to 3 years of age, 5 of the 50 female triploid salmon recipients ovulated eggs (table S2) that were then fertilized with milt harvested from the male triploid salmon recipients. Although developmental rates of the offspring varied from one female broodstock to the next, the hatching rate reached 89.5% (table S2). The ratios of orange-colored trout to wild-type trout and of p*vasa-Gfp*(+) to p*vasa-Gfp*(–) were both about 3:1 in the F_1 generation (Fig. 1C and table S3). These findings show Mendelian inheritance of *OR*/*WT* and p*vasa-Gfp*/–, implying that the F_1 generation was produced from donor-derived sperm and eggs. Resulting fry also developed normally (Fig. 1D). Restriction fragment length polymorphism (RFLP) analysis of mitochondrial DNA revealed that all F_1 fish specimens examined (n = 18) carried trout mitochondria (fig. S3). Thus, female triploid salmon recipients that received trout spermatogonia produced only donor-derived trout eggs. In addition, RAPD analysis of total DNA showed that the DNA fingerprinting pattern of the F_1 generation was the same as that of trout (fig. S3). Further, the F_1 generation was fertile and could produce normal F_2 trout. We therefore established a surrogate broodstock technique for salmonids in which spermatogonia can be transplanted into sterile triploid xenogeneic recipients to produce a next generation consisting entirely of donor-derived fish. We also confirmed that trout spermatogonia frozen in a cryomedium had a high associated survival rate (45.4%). Thus, by transplanting cryopreserved spermatogonia into sterile xenogeneic recipients, it is possible to generate individuals of an endangered, and perhaps extinct, species.

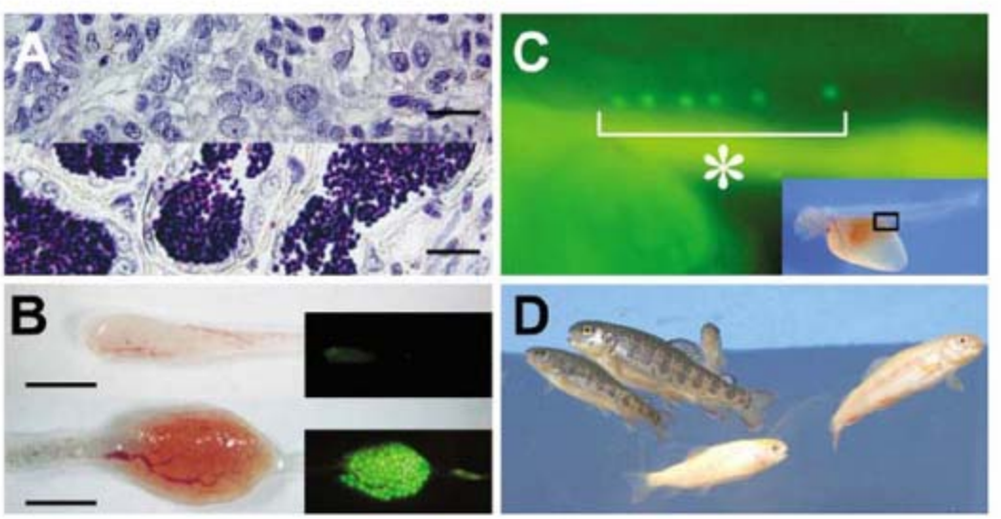

Fig. 1. Development of donor-derived germ cells and F1 offspring generated from surrogate parents. **(A)** Hematoxylin and eosin (H&E)–stained section of testes from an intact triploid salmon (top) and a triploid salmon recipient that received spermatogonial transplantation (bottom). Scale bars indicate 20 μm. **(B)** Oocyte colony derived from donor trout spermatogonia in the ovary of triploid salmon recipient at 17 months after transplantation (bottom) and ovaries of intact triploid salmon (top) at the same age as the recipient. (Insets) Fluorescent views. Scale bars, 5 mm. **(C)** Lateral view of orange-colored offspring (inset), with a highly magnified image of a frame. *Gfp* was expressed in PGCs (asterisk). **(D)** Trout juveniles at 6 months old generated from surrogate triploid salmon parents.

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Supporting Online Material

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Materials and Methods
Figs. S1 to S3
Tables S1 to S3
References

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Checkers Is Solved

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Martin Müller, Robert Lake, Paul Lu, Steve Sutphen

The game of checkers has roughly 500 billion billion possible positions (5×10^{20}). The task of solving the game, determining the final result in a game with no mistakes made by either player, is daunting. Since 1989, almost continuously, dozens of computers have been working on solving checkers, applying state-of-the-art artificial intelligence techniques to the proving process. This paper announces that checkers is now solved: Perfect play by both sides leads to a draw. This is the most challenging popular game to be solved to date, roughly one million times as complex as Connect Four. Artificial intelligence technology has been used to generate strong heuristic-based game-playing programs, such as Deep Blue for chess. Solving a game takes this to the next level by replacing the heuristics with perfection.

Since Claude Shannon's seminal paper on the structure of a chess-playing program in 1950 (*1*), artificial intelligence researchers have developed programs capable of challenging and defeating the strongest human players in the world. Superhuman-strength programs exist for popular games such as chess [Deep Fritz (*2*)], checkers [Chinook (*3*)], Othello [Logistello (*4*)], and Scrabble [Maven (*5*)]. However strong these programs are, they are not perfect. Perfection implies solving a game—determining the final result (game-theoretic value) when neither player makes a mistake. There are three levels of solving a game (*6*). For the lowest level, ultraweakly solved, the perfect-play result, but not a strategy for achieving that value, is known [e.g., in Hex the first player wins, but for large board sizes the winning strategy is not known (*7*)]. For weakly solved games, both the result and a strategy for achieving it from the start of the game are known [e.g., in Go Moku the first player wins and a program can demonstrate the win (*6*)]. Strongly solved games have the result computed for all possible positions that can arise in the game [e.g., Awari (*8*)].

Checkers (8×8 draughts) is a popular game enjoyed by millions of people worldwide, with many annual tournaments and a series of competitions that determine the world champion. There are numerous variants of the game played around the world. The game that is popular in North America and the (former) British Commonwealth has pieces (checkers) moving forward one square diagonally, kings moving forward or backward one square diagonally, and a forced-capture rule [see supporting online material (SOM) text].

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The effort to solve checkers began in 1989, and the computations needed to achieve that result have been running almost continuously since then. At the peak in 1992, more than 200 processors were devoted to the problem simultaneously. The end result is one of the longest running computations completed to date.

With this paper, we announce that checkers has been weakly solved. From the starting position (Fig. 1, top), we have a computational proof that checkers is a draw. The proof consists of an explicit strategy that never loses—the program can achieve at least a draw against any opponent, playing either the black or white pieces. That checkers is a draw is not a surprise; grandmaster players have conjectured this for decades.

The checkers result pushes the boundary of artificial intelligence (AI). In the early days of AI research, the easiest path to achieving high performance was believed to be emulating the human approach. This was fraught with difficulty, especially the problems of capturing and encoding human knowledge. Human-like strategies are not necessarily the best computational strategies. Perhaps the biggest contribution of applying AI technology to developing game-playing programs was the realization that a search-intensive ("brute-force") approach could produce high-quality performance using minimal application-dependent knowledge. Over the past two decades, powerful search techniques have been developed and successfully applied to problems such as optimization, planning, and bioinformatics. The checkers proof extends this approach by developing a program that has little need for application-dependent knowledge and is almost completely reliant on search. With advanced AI algorithms and improved hardware (faster processors, larger memories, and larger disks), it has become possible to push the limits on the type and size of problems that can be solved. Even so, the checkers search space (5×10^{20}) represents a daunting challenge for today's technology.

Computer proofs in areas other than games have been done numerous times. Perhaps the best known is the four-color theorem (*9*). This deceptively simple conjecture—that given an arbitrary map with countries, you need at most four different colors to guarantee that no two adjoining countries have the same color—has been extremely difficult to prove analytically. In 1976, a computational proof was demonstrated. Despite the convincing result, some mathematicians were skeptical, distrusting proofs that had not been verified using human-derived theorems. Although important components of the checkers proof have been independently verified, there may be skeptics.

This article describes the background behind the effort to solve checkers, the methods used for achieving the result, an argument that the result is correct, and the implications of this research. The computer proof is online (*10*).

Background. The development of a strong checkers program began in the 1950s with Arthur Samuel's pioneering work in machine learning. In 1963, his program played a match against a capable player, winning a single game. This result was heralded as a triumph for the fledgling field of AI. Over time, the result was exaggerated, resulting in claims that checkers was now "solved" (*3*).

The Chinook project began in 1989 with the goal of building a program capable of challenging the world checkers champion. In 1990, Chinook earned the right to play for the World Championship. In 1992, World Champion Marion Tinsley narrowly defeated Chinook in the title match. In the 1994 rematch, Tinsley withdrew part way due to illness. He passed away eight months later. By 1996 Chinook was much

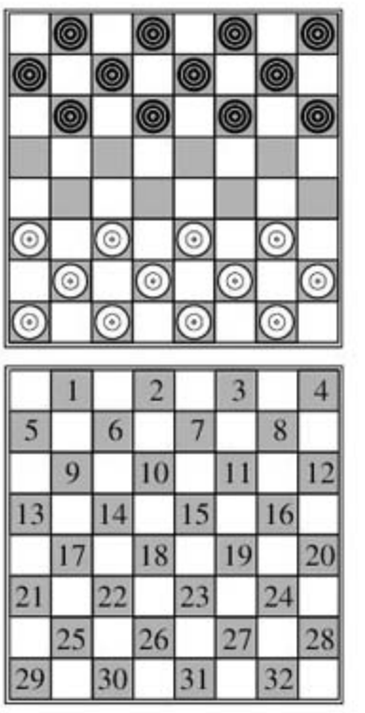

Fig. 1. Black to play and draw. **(Top)** Standard starting board. **(Bottom)** Square numbers used for move notation.

stronger than all human players, and with faster processors this gap has only grown (*3*).

Tinsley was the greatest checkers player that ever lived, compiling an incredible record that included only three losses in the period from 1950 to 1991. The unfinished Tinsley match left the question unanswered as to who was the better player. If checkers were a proven draw, then a "perfect" Chinook would never lose. As great as Tinsley was, he did occasionally make losing oversights. Hence, solving checkers would once and for all establish computers as better checkers players than all (fallible) humans.

Numerous nontrivial games have been solved, including Connect Four (*6*, *11*), Qubic (*6*), Go-Moku (*6*), Nine Men's Morris (*12*), and Awari (*8*). The perfect-play result and a strategy for achieving that result is known for these games. How difficult is it to solve a game? There are two dimensions to consider (*6*): (i) decision complexity, the difficulty of making correct move decisions, and (ii) space complexity, the size of the search space.

Checkers is considered to have high decision complexity (it requires extensive skill to make strong move choices) and moderate space complexity (5×10^{20}) (Table 1). All the games solved thus far have either low decision complexity (Qubic and Go-Moku), low space complexity (Nine Men's Morris, size 10^{11}, and Awari, size 10^{12}), or both (Connect Four, size 10^{14}).

Solving checkers. Checkers represents the most computationally challenging game solved to date. The proof procedure has three algorithm/data components (*13*): (i) Endgame databases (backward search). Computations from the end of the game back toward the starting position have resulted in a database of 3.9×10^{13} positions (all positions with ≤10 pieces on the board) for which the game-theoretic value has been computed (strongly solved). (ii) Proof-tree manager (forward search). This component maintains a tree of the proof in progress (a sequence of moves and their best responses), traverses it, and generates positions that need to be explored to further the proof's progress. (iii) Proof solver (forward search). Given a position to search by the manager, this component uses two programs to determine the value of the position. These programs approach the task in different ways, thus increasing the chances of obtaining a useful result. Figure 2 shows the forward and backward search interactions in the checkers search space.

In the manager, the proof tree can be hand-seeded with an initial line of play. From the literature (*14*), a single "best" line of play was identified and used to guide the initial foray of the manager into the depths of the search tree. Although not essential for the proof, this is an important performance enhancement. It allows the proof process to immediately focus its work on the parts of the search space that are likely to be relevant. Without it, the manager may spend unnecessary effort looking for an important line to explore. The line leads from the start of the game into the endgame databases (Fig. 2).

Backward search. Positions at the end of the game can be searched and their win/loss/draw value determined. The technique is called retrograde analysis and has been successfully used for many games. The algorithm works backward by starting at the end of the game and working toward the start. It enumerates all one-piece positions, determining their value (in this case, a trivial win for the side with the piece). Next, all two-piece positions are enumerated and analyzed. The analysis for each position eventually leads to a one-piece position with a known value, or a repeated position (draw). Next, all the three-piece positions are tackled, and so forth (SOM text). Our program has computed all the positions with ≤10 pieces on the board. The endgame databases are crucial to solving checkers. The checkers forced-capture rule quickly results in many pieces being removed from the board, giving rise to a position with ≤10 pieces—and a known value.

The databases contain the win/loss/draw result for a position, not the number of moves to a win/

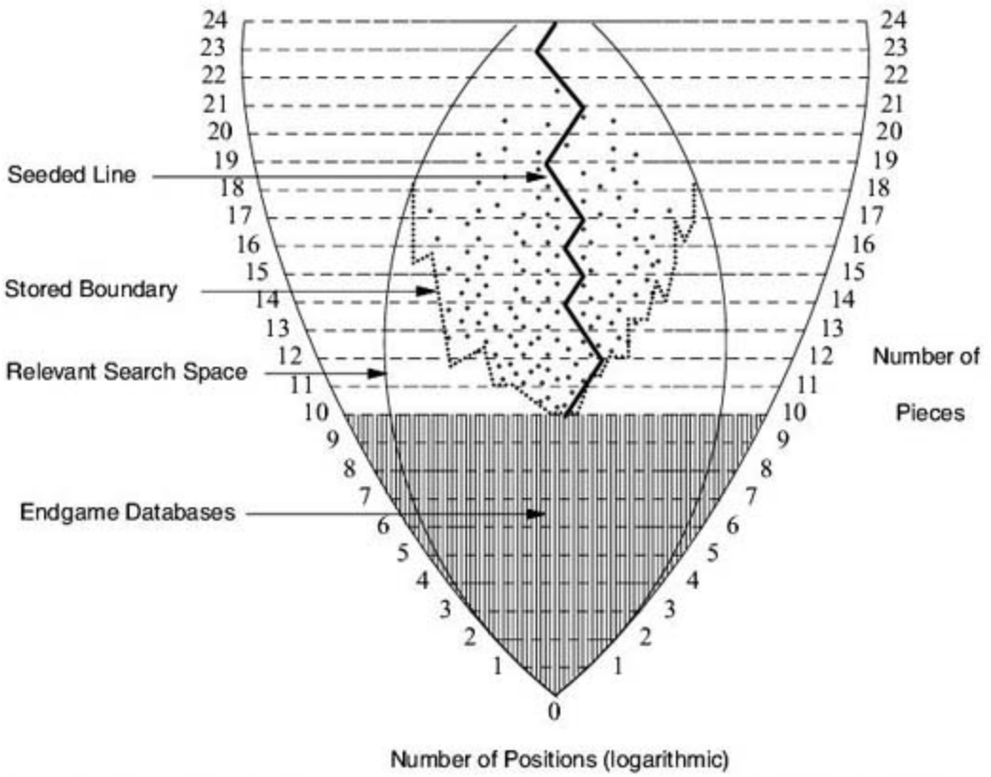

Fig. 2. Forward and backward search. The number of pieces on the board are plotted (vertically) versus the logarithm of the number of positions (Table 1). The shaded area shows the endgame database part of the proof—i.e., all positions with ≤10 pieces. The inner oval area shows that only a portion of the search space is relevant to the proof. Positions may be irrelevant because they are unreachable or are not required for the proof. The small open circles indicate positions with more than 10 pieces for which a value has been proven by a solver. The dotted line shows the boundary between the top of the proof tree that the manager sees (and stores on disk) and the parts that are computed by the solvers (and are not saved in order to reduce disk storage needs). The solid seeded line shows a "best" sequence of moves.

Table 1. The number of positions in the game of checkers. For example, the possible positions for one piece include 32 squares for the Black king, 32 squares for the White king, 28 squares for a Black checker, and 28 squares for a White checker, for a total of 120 positions.

Pieces	Number of positions
1	120
2	6,972
3	261,224
4	7,092,774
5	148,688,232
6	2,503,611,964
7	34,779,531,480
8	406,309,208,481
9	4,048,627,642,976
10	34,778,882,769,216
Total 1–10	39,271,258,813,439
11	259,669,578,902,016
12	1,695,618,078,654,976
13	9,726,900,031,328,256
14	49,134,911,067,979,776
15	218,511,510,918,189,056
16	852,888,183,557,922,816
17	2,905,162,728,973,680,640
18	8,568,043,414,939,516,928
19	21,661,954,506,100,113,408
20	46,352,957,062,510,379,008
21	82,459,728,874,435,248,128
22	118,435,747,136,817,856,512
23	129,406,908,049,181,900,800
24	90,072,726,844,888,186,880
Total 1–24	500,995,484,682,338,672,639

loss. Independent research has discovered a 10-piece database position requiring a 279-ply move sequence to demonstrate a forced win (a ply is one move by one player) (*15*). This is a conservative bound; the win length has not been computed for the more difficult (and more interesting) database positions.

The complete 10-piece databases contain 39 trillion positions (Table 1). They are compressed into 237 gigabytes, an average of 154 positions per byte. A custom compression algorithm was used that allows for rapid localized real-time decompression (*16*). This means that the backward and forward search programs can quickly extract information from the databases.

The first databases, constructed in 1989, were for less than or equal to four pieces. In 1994, Chinook used a subset of the eight-piece database for the Tinsley match (*3*). By 1996, the eight-piece database was completed, giving rise to hope that checkers could be solved. However, the problem was still too hard, and the effort came to a halt. In 2001, computer capabilities had increased substantially, and the effort was restarted. It took 7 years (1989 to 1996) to compute the original eight-piece databases; in 2001 it took only a month. In 2005, the 10-piece database computation finished. At this point, all computational resources were focused on the forward search effort.

Forward search. Development of the forward search program began in 2001, with the production version up and running in 2004. The forward search consists of two parts: the proof-tree manager, which builds the proof by identifying positions that need to be assessed, and the proof solvers, which search individual positions.

The manager maintains the master copy of the proof and uses the Proof Number search algorithm (*6*) to identify a prioritized list of positions that need to be examined. Typically, several hundred positions of interest are generated at a time so as to keep multiple computers busy. Over the past year, we used an average of 50 computers simultaneously.

The solvers get a position to evaluate from the manager. The result of a position evaluation can be proven (win, loss, or draw), partially proven (at least a draw, at most a draw), or heuristic (an estimate of how good or bad a position is). Proven positions need no further work; partially proven positions need additional work if the manager determines that a proven value is needed. If no proven information is available then the solver returns a heuristic assessment of the position. The manager uses this assessment to prioritize which positions to consider next. The manager updates the proof tree with the new information, decides which positions need further investigation, and generates new work to do. This process is repeated until a proven result for the game is determined.

The solver uses two search programs to evaluate a position. The first program (targeted at 15 s, but sometimes much longer) uses Chinook to determine a heuristic value for the position (alpha-beta search to nominal search depths of 17 to 23 ply). Occasionally, this search determines that the position is a proven win or loss. Chinook was not designed to produce a proven draw, only a heuristic draw; demonstrating proven draws in a heuristic search seriously degrades performance.

The alpha-beta search algorithm is the mainstay of game-playing programs. The algorithm does a depth-first, left-to-right traversal of the search tree (*17*) (SOM text). The algorithm propagates heuristic bounds on the value of a position: the minimum value that the side about to move can achieve and the maximum value that the side about to move can be limited to by the opponent. Lines of play that are provably outside this range are irrelevant and can be eliminated (cut off). A d-ply search with an average of b moves to consider in every position results in a tree with roughly b^d positions. In the best case, the alpha-beta algorithm only needs to examine roughly $b^{d/2}$ positions (*16*).

If Chinook does not find a proven result, then a second program is invoked (100 s). It uses the Df-pn algorithm (*18*), a space-efficient variant of Proof Number search. The search returns a proven, partially proven, or unknown result.

Algorithms based on proof numbers maintain a measure of the difficulty of proving a position. This difficulty is expressed as a proof number, a lower bound on the minimum number of positions that need to be explored to result in the position being proven. The algorithm repeatedly expands the tree below the position requiring the least effort to affect the original position (a "best-first" approach). The result of that search is propagated back up the tree, and a new best candidate to consider is determined. Proof number search was specifically invented to facilitate the proving of games. The Df-pn variant builds the search tree in a depth-first manner, requiring less computer storage.

Iterative search algorithms are commonplace in the AI literature. Most iterate on search depth (first 1 ply, then 2, then 3, etc.). The manager uses the new approach of iterating on the error in Chinook's heuristic scores (*13*). The manager uses a threshold, t, and temporarily assumes that all heuristic scores $\geq t$ are wins and all scores $\leq -t$ are losses. It then proves the result given this assumption. Once completed, t is increased to $t+\Delta$, and the process is repeated. Eventually t reaches the value of a win and the proof is complete. This iterative approach concentrates the effort on forming the outline of the proof with low values of t, and then fleshing out the details with the rest of the computation.

One complication is the graph-history interaction (GHI) problem. It is possible to reach the same position through two different sequences of moves. This means that some draws depend on the moves played leading to the duplicated position. In standard search algorithms, GHI may cause some positions to be incorrectly inferred as draws. Part of this research project was to develop an improved algorithm for addressing the GHI problem (*19*).

Correctness. Given a computation that has run for so long on many processors, an important

Table 2. Openings solved. Shown are the opening moves (using the standard square number scheme in Fig. 1, bottom), the result, the number of positions given to the solvers, and the position farthest from the start of the game that was searched (Max ply). The last two columns give the size and ply depth of the pruned minimal proof tree. Note that the total does not match the sum of the 19 openings. The combined tree has some duplicated nodes, which have been removed when reporting the total.

No.	Opening	Proof	Searches	Max ply	Minimal size	Max ply
1	09-13 22-17 13-22	Draw	736,984	56	275,097	55
2	09-13 21-17 05-09	Draw	1,987,856	154	684,403	85
3	09-13 22-18 10-15	Draw	715,280	103	265,745	58
4	09-13 23-18 05-09	Draw	671,948	119	274,376	94
5	09-13-23-19 11-16	Draw	964,193	85	358,544	71
6	09-13 24-19 11-15	Draw	554,265	53	212,217	49
7	09-13 24-20 11-15	Draw	1,058,328	59	339,562	58
8	09-14 23-18 14-23	≤Draw	2,202,533	77	573,735	75
9	10-14 23-18 14-23	≤Draw	1,296,790	58	336,175	55
10	10-15 22-18 15-22	≤Draw	543,603	60	104,882	41
11	11-15 22-18 15-22	≤Draw	919,594	67	301,310	59
12	11-16 23-19 16-23	≤Draw	1,969,641	69	565,202	64
13	12-16 24-19 09-13	Loss	205,385	44	49,593	40
14	12-16 24-19 09-14	≤Draw	61,279	45	23,396	44
15	12-16 24-19 10-14	≤Draw	21,328	31	8,917	31
16	12-16 24-19 10-15	≤Draw	31,473	35	13,465	35
17	12-16 24-19 11-15	≤Draw	23,803	34	9,730	34
18	12-16 24-19 16-20	≤Draw	283,353	49	113,210	49
19	12-16 24-19 08-12	≤Draw	266,924	49	107,109	49
Overall		Draw	Total	Max	Total	Max
			15,123,711	154	3,301,807	94

question to ask is "Are the results correct?" Early on in the computation, we realized that there were many potential sources of errors, including algorithm bugs and data transmission errors. Great care has been taken to eliminate any possibility of error by verifying all computation results and doing consistency checks. As well, some of the computations have been independently verified (SOM text).

Even if an error has crept into the calculations, it likely does not change the final result. Assume a position that is 40 ply away from the start is incorrect. The probability that this erroneous result can propagate up 40 ply and change the value for the game of checkers is vanishingly small (*20*).

Results. Our approach to solving the game was to determine the game-theoretic result by doing the least amount of work. In tournament checkers, the standard starting position (Fig. 1, top) is considered "boring," so the first three moves (ply) of a game are randomly chosen at the start. The checkers proof consisted of solving 19 three-move openings, leading to a determination of the starting position's value: a draw. Although there are roughly 300 three-move openings, more than 100 are duplicates (move transpositions). The rest can be proven to be irrelevant by an alpha-beta search.

Table 2 shows the results for the 19 openings solved to determine the perfect-play result for checkers. (Other openings have been solved but are not included here.) After an opening was proven, a postprocessing program pruned the tree to eliminate all the computations that were not part of the smallest proof tree. In hindsight, the pruned work was unnecessary, but it was not so at the time when it was assigned for evaluation. Figure 3 shows the proof tree for the first 3 ply.

The leftmost move sequence in Fig. 3 is as follows: Black moves from 09 to 13 (represented using the standard checkers notation 09-13), White replies with 22-17, and then Black moves 13-22. The resulting position has been searched and shown to be a draw (opening line 1 in Fig. 3). That means the position after 22-17 is also a draw, given that there is only one legal move available (13-22) and it is a proven draw. What is the value of the position after Black moves 09-13? To determine this, all possible moves for White have to be considered. The move 22-17 guarantees White at least a draw (at most a draw for Black). But it is possible that this position is a win for White (and a loss for Black). The remaining moves (21-17, 22-18, 23-18, 23-19, 24-19, and 24-20; opening lines 2 to 7 in Fig. 3) are all shown to be at least a draw for Black. Hence, White prefers the move 22-17 (no worse than any other move). Thus, 09-13 leads to a draw (White will move 22-17 in response).

Given that 09-13 is a draw, it remains to demonstrate that the other opening moves cannot win for Black. Note that some openings have a proven result, whereas for others only the partial result that was necessary for the proof was computed. The number of openings is small because the forced-capture rule was exploited. Opening lines 13 to 19 in Fig. 3 are needed to prove that the opening 12-16 is not a win. Actually, one opening would have sufficed (12-16, 23-19, and 16-23). However, human analysts consider this line to be a win for Black, and the preliminary analysis agreed. Hence, the seven openings beginning with the moves 12-16 and 24-19 were proven instead. This led to the least amount of computing.

There is anecdotal evidence that the proof tree is correct. Main lines of play were manually compared to human analysis (*14*), with no errors found in the computer's results (unimportant errors were found in the human analysis).

The proof tree shows the perfect lines of play needed to achieve a draw. If one side makes a losing mistake, the proof tree may not necessarily show how to win. This additional information is not necessary for proving the draw result.

The stored proof tree is only 10^7 positions. Saving the entire proof tree, from the start of the game so that every line ends in an endgame database position, would require many tens of terabytes, resources that were not available. Instead, only the top of the proof tree, the information maintained by the manager, is stored on disk. When a user queries the proof, if the end of a line of play in the proof is reached, then the solver is used to continue the line into the databases. This substantially reduces the storage needs, at the cost of recomputing (roughly 2 min per search).

The longest line analyzed was 154 ply. The position at the end of this line was analyzed by the solver, and that analysis may have gone 20 or more ply deep. At the end of this analysis is a database position, which could be the result of several hundred ply of analysis. This provides supporting evidence of the difficulty of checkers—for computers and humans.

How much computation was done in the proof? Roughly speaking, there are 10^7 positions in the stored proof tree, each representing a search of 10^7 positions (relatively small because of the extensive disk operations). Hence, 10^{14} is a good ballpark estimate of the forward search effort.

Should we be impressed with "only" 10^{14} computations? At one extreme, checkers could be solved using storage—build endgame databases for the complete search space. This would require 5×10^{20} data entries. Even an excellent compression algorithm might only reduce this to 10^{18} bytes, impractical with today's technology. This also makes it unlikely that checkers will soon be strongly solved.

An alternative would be to use only computing—i.e., build a search tree using the alpha-beta algorithm. Consider the following unreasonably optimistic assumptions: number of moves to consider is eight in noncapture positions, a game lasts 70 ply, all captures are of a single piece (23 capture moves), and the alpha-beta search does the least possible work. The assumptions result in a search tree of $8^{(70-23)} = 8^{47}$ states. The perfect alpha-beta search will halve the exponent, leading to a search of roughly $8^{47/2} \approx 10^{24}$. This would take more than a lifetime to search, given current technology.

Conclusion. What is the scientific significance of this result? The early research was devoted to developing Chinook and demonstrating superhuman play in checkers, a milestone that predated the Deep Blue success in chess. The project has been a marriage of research in AI and parallel computing, with contributions made in both of these areas. This research has been used by a bioinformatics company; real-time access of very large data sets for use in parallel search is as relevant for solving a game as it is for biological computations.

The checkers computation pushes the boundary of what can be achieved by search-intensive algorithms. It provides compelling evidence of the power of limited-knowledge approaches to artificial intelligence. Deep search implicitly uncovers knowledge. Furthermore, search algorithms are well poised to take advantage of the

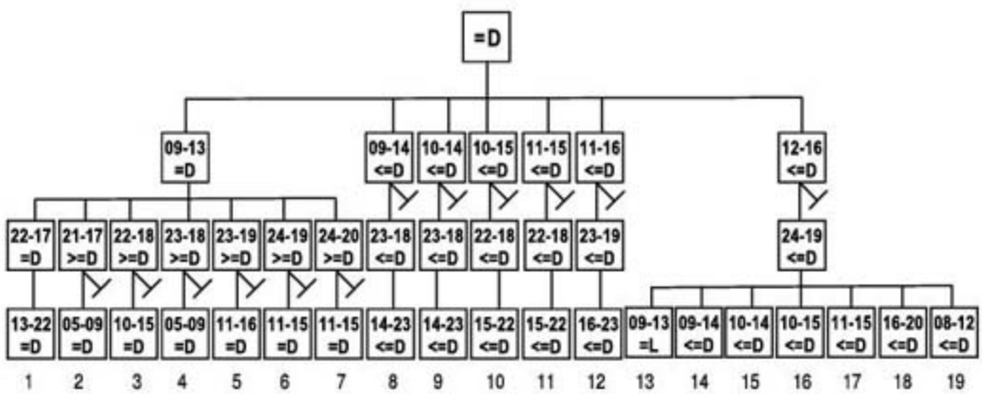

Fig. 3. The first three moves of the checkers proof tree. Move sequences are indicated using the notation from Fig. 1B, with the from-square and to-square of the move separated by a hyphen. The result of each position is given for Black, the first player to move (=D, a proven draw; =L, a proven loss; <=D, loss or draw; and >=D, draw or win). In some positions, only one move needs to be considered; the rest are cut off, as indicated by the rotated "T". Some positions have only one legal move because of the forced-capture rule.

increase in on-chip parallelism that multicore computing will soon offer. Search-intensive approaches to AI will play an increasingly important role in the evolution of the field.

With checkers finished, the obvious question is whether chess is solvable. Checkers has roughly the square root of the number of positions in chess (somewhere in the 10^{40} to 10^{50} range). Given the effort required to solve checkers, chess will remain unsolved for a long time, barring the invention of new technology. The disk-flipping game of Othello is the next popular game that is likely to be solved, but it will require considerably more resources than were needed to solve checkers (*7*).

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Supporting Online Material

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Figs. S1 to S4
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TLR3 Deficiency in Patients with Herpes Simplex Encephalitis

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Some Toll and Toll-like receptors (TLRs) provide immunity to experimental infections in animal models, but their contribution to host defense in natural ecosystems is unknown. We report a dominant-negative *TLR3* allele in otherwise healthy children with herpes simplex virus 1 (HSV-1) encephalitis. TLR3 is expressed in the central nervous system (CNS), where it is required to control HSV-1, which spreads from the epithelium to the CNS via cranial nerves. TLR3 is also expressed in epithelial and dendritic cells, which apparently use TLR3-independent pathways to prevent further dissemination of HSV-1 and to provide resistance to other pathogens in TLR3-deficient patients. Human TLR3 appears to be redundant in host defense to most microbes but is vital for natural immunity to HSV-1 in the CNS, which suggests that neurotropic viruses have contributed to the evolutionary maintenance of TLR3.

The contribution of Toll and Toll-like receptors to immunity has been studied extensively in the past decade. Toll-deficient *Drosophila* were shown to be susceptible to experimental infections with certain fungi in 1996 (*1*), and a Toll-like receptor 4 (TLR4) null mutation in mice resistant to lipopolysaccharide (LPS) but susceptible to certain Gram-negative bacteria was identified in 1998 (*2*). Mice deficient for individual TLRs have since been generated and shown to have diverse infectious phenotypes, from susceptibility to resistance, depending on the TLR-pathogen combination (*3*). However, it remains unclear whether TLRs play nonredundant roles—beneficial or detrimental—in natural, as opposed to experimental, infections. This biological question is important, because natural selection acts on a given species in the setting of natural (rather than experimental) ecosystems. The human model is particularly suitable for analyses of the relevance of genes such as those of TLRs to host defense in natural ecosystems (*4*). Nevertheless, although many studies have suggested that TLR genes are involved in human infectious diseases, this has not been unambiguously demonstrated (*5*). In particular, no primary immunodeficiency involving TLRs has been identified.

The discovery of inherited interleukin 1 receptor-associated kinase-4 (IRAK-4) deficiency in children with bacterial diseases implicated human TLRs, interleukin-1 receptors (IL-1Rs), or both in host defense (*6*, *7*). However, the narrow range of infections documented in such patients indicates that IRAK-4–dependent, TLR-mediated immunity is redundant for protective immunity to most microbes. In particular, IRAK-4–deficient patients are not susceptible to herpes simplex virus 1 (HSV-1) encephalitis (HSE). In HSE, HSV-1 infects epithelial cells in the oral and nasal mucosa and progresses to the central nervous system (CNS) via the trigeminal or olfactory nerves (*8*). A genetic etiology of HSE was found in two children who lacked functional UNC-93B (*9*), an endoplasmic reticulum protein required for TLR3, TLR7, TLR8, and TLR9 signaling (*10*). Both UNC-93B– and IRAK-4–deficient patients fail to signal through TLR7, TLR8, and TLR9, but unlike IRAK-4–deficient patients (*7*), UNC-93B–deficient patients display impaired TLR3-dependent interferon-α (IFN-α) -β, and -λ production (*9*). Moreover, HSV-1 is a double-stranded DNA virus with double-stranded RNA (dsRNA) intermediates (*11*), and TLR3 recog-

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nizes dsRNA (*12*). Finally, TLR3 is expressed in CNS-resident cells (*13*–*15*) and peripheral nerves (*16*). Collectively, these observations suggest that impaired TLR3-dependent induction of IFN-α, -β and -λ might be involved in HSE.

A heterozygous TLR3 mutation in two children with HSE. We investigated two unrelated French children (P1 and P2) with HSE (SOM Text, note 2). UNC-93B deficiency was excluded on genetic and immunological grounds (fig. S1, A to D). Leukocytes and fibroblasts from P1 and P2 harbored the same heterozygous substitution (C→T) in *TLR3* at nucleotide position 1660 (c.1660C>T) (Fig. 1, A and B). The two kindreds represent independent mutational events because the two P554S mutations were in different *TLR3* haplotypes. The mutation leads to the replacement of a proline (P) by a serine (S) at residue 554 (P554S) (Fig. 1C). P554S has not previously been described (*17*, *18*) and was not found in any of the 1581 unrelated healthy individuals examined (3162 chromosomes), including 241 Europeans. Residue P554 of TLR3 is conserved in the 18 animal species studied (Fig. 1D). The extracellular, ligand-binding domain of TLR3 contains 23 contiguous leucine-rich repeats (LRRs) forming a large, horseshoe-shaped solenoid (Fig. 1E) (*19*). P554 anchors the TLR3-specific insertion of residues 544 to 554 in LRR20 (Fig. 1E) (*19*, *20*). This region is thought to be critical for dsRNA binding to TLR3 (*20*) and TLR3 multimerization (*19*). Three relatives of P1 and two of P2 were also heterozygous for the mutation (Fig. 1A). They were HSV-1 seropositive but had not suffered from HSE, which suggests that the P554S TLR3 mutation conferred an autosomal dominant predisposition to HSE with incomplete clinical penetrance.

Impaired responsiveness of fibroblasts to poly(I:C) stimulation. We derived dermal fibroblastic cell lines, which selectively express TLR3 (*9*), from patients and controls. The TLR3 agonist polyinosine-polycytidylic acid [poly(I:C)], which mimics dsRNA (*12*), induced IFN-β, -λ, and IL-6 in a dose- and time-dependent manner in all control fibroblasts but not in the TLR3-deficient fibrosarcoma P2.1 cell line (SOM Text, note 1) (Fig. 2A and fig. S2A). Primary and simian virus 40 (SV40)–transformed fibroblasts from P1 and P2 displayed only a residual response at high concentrations of poly(I:C) and late time points (Fig. 2A). IL-6 induction was less impaired. The induction of IFN-β and -λ mRNA production by poly(I:C) was markedly weaker in P1 fibroblasts (fig. S2B). Both nuclear factor kappa B (NF-κB) (Fig. 2B) and IFN regulatory factor-3 (IRF-3) (Fig. 2C) activation were impaired in response to poly(I:C) in the patients' fibroblasts, which responded normally to tumor necrosis factor–α (TNF-α) and IL-1β (Fig. 2B and fig. S2C). NF-κB essential modulator (NEMO)–deficient fibroblasts (SOM Text, note 1) did not respond to poly(I:C), IL-1β, or TNF-α (Fig. 2B), and UNC-93B–deficient fibroblasts (*9*) did not respond to poly (I:C) (Fig. 2C). Finally, all tested relatives carrying the TLR3 mutation, but none of the relatives without this mutation, displayed impaired responses to poly(I:C) (fig. S2D). The cosegregation of genotype and fibroblastic phenotype suggests that heterozygosity for the P554S *TLR3* allele confers autosomal dominant hyporesponsiveness to poly(I:C) in fibroblasts.

Dominant-negative effect of the P554S *TLR3* allele in fibroblasts. TLR3 multimerizes upon binding dsRNA, and several TLR3 mutants are dominant negative (*20*–*22*), which suggests that the P554S mutation may be dominant negative. *TLR3* mRNA is produced in normal quantities (Fig. 2D) in the patients' fibroblasts (fig. S2E), and the wild-type (WT) and P554S *TLR3* mRNAs were equally abundant (fig. S2F). Stable transfection of P2.1 cells with C-terminal

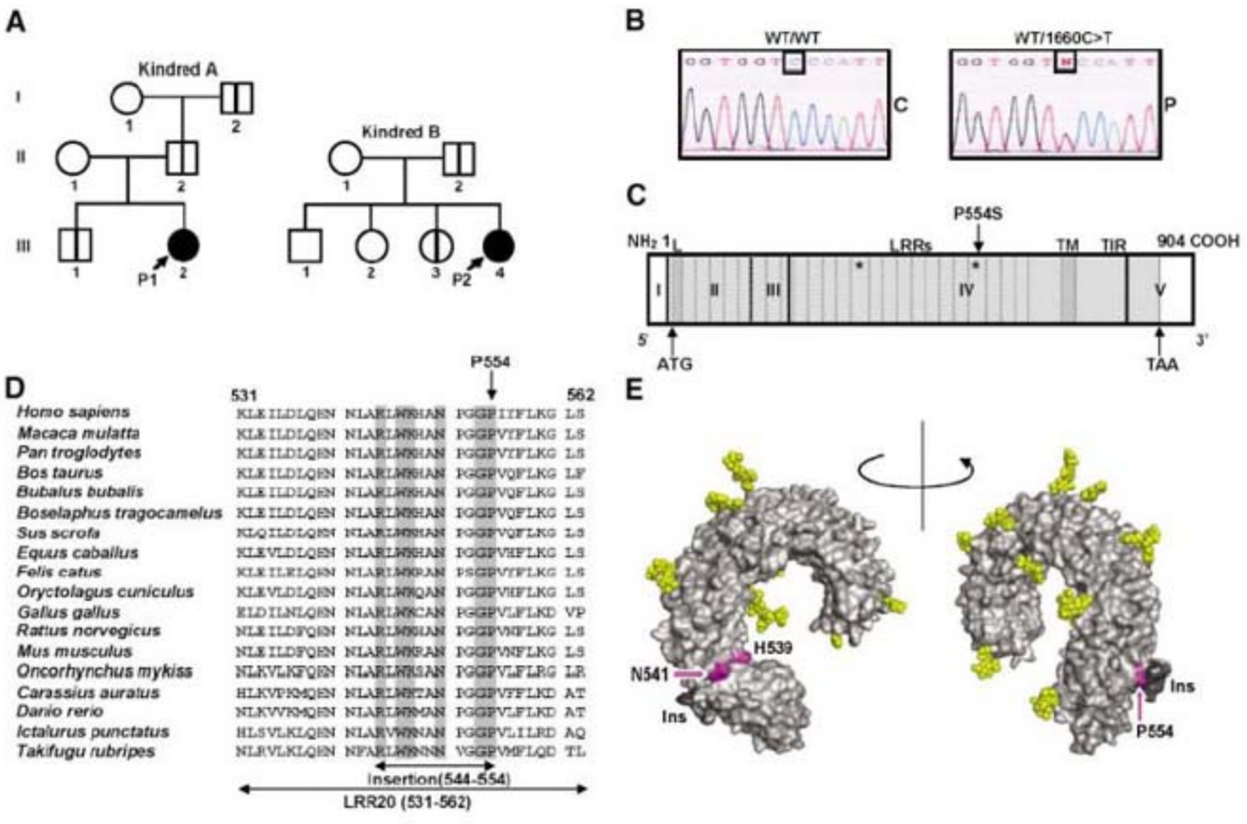

Fig. 1. Heterozygous TLR3 P554S mutation in two unrelated children with HSE. **(A)** Family pedigrees, with allele segregation in the two families. The patients, in black, are heterozygous for the mutation. The other family members heterozygous for the mutation are indicated by bold vertical lines. **(B)** Heterozygous c.1660C>T mutation in the patients. The sequence of the polymerase chain reaction products of genomic DNA from leukocytes of a control (C) and P1 (P) is shown. The mutation was confirmed in genomic DNA and cDNA from leukocytes and fibroblasts. **(C)** Schematic representation of *TLR3* gene structure. Human *TLR3* has five exons (Roman numerals) encoding a protein (shown in gray) composed of a leader sequence (L), an LRR domain, a transmembrane (TM) domain, and a Toll/interleukin-1 receptor (TIR) domain. The various LRR motifs, the N-terminal cap, and the C-terminal cap of the LRR domain are separated by dotted vertical lines, and the two LRRs with an insertion are indicated by asterisks. The c.1660C>T mutation results in a proline (P) to serine (S) substitution at amino acid position 554 (P554S) in LRR20. **(D)** LRR20 of TLR3 in humans and the corresponding region in the other 17 species studied, with the insertion indicated. The amino acids conserved in the insertion in all these species are shaded in gray. **(E)** Two views of the human TLR3 ectodomain (ECD) surface. H539 and N541 (left), implicated in ligand binding, and P554 (right) are shown in magenta. "Ins" refers to the eight residues from W546 to G553 in the TLR3-specific insertion 544 to 554 of the LRR20, and is shown in dark gray. Glycan is shown in yellow, and the C terminus of the TLR3 ECD is at the bottom.

hemagglutinin (HA)–tagged WT *TLR3*, but not with P554S *TLR3*, restored the cell response to poly(I:C), as measured by IFN-β (fig. S2G) and IFN-λ production (Fig. 2E). Both WT and P554S *TLR3* mRNAs were detected (Fig. 2F). The P554S TLR3 protein had a lower molecular weight than the WT, as shown by Western blotting with two antibodies that specifically recognize the TLR3 N-terminal ectodomain, but not with an antibody to C-terminal–tagged HA (Fig. 2G). Upon transient transfection of control fibroblasts with various ratios of mock vector and P554S *TLR3* allele, the response to poly(I:C) decreased as the proportion of P554S *TLR3* allele increased (fig. S2H). Moreover, control fibroblasts stably transfected with the P554S *TLR3* allele lost their ability to respond to poly(I:C) (Fig. 2H). These observations were extended to P2.1 recipient cells (SOM Text, note 3). The P554S TLR3 protein is thus C-terminally truncated, loss-of-function for poly(I:C) responsiveness, and dominant negative in dermal fibroblasts and the fibrosarcoma P2.1 cell line, at least for IFN induction.

Impaired IFN-dependent control of viruses in TLR3-deficient fibroblasts. UNC-93B–deficient fibroblasts produce little IFN-β and -λ upon viral stimulation, resulting in high levels of viral replication and cell death (*9*). We therefore infected TLR3-heterozygous fibroblasts with HSV-1 and another neurotropic virus, vesicular stomatitis virus (VSV)—a highly cytopathic virus and potent IFN inducer in human fibroblasts. IFN-β and -λ production after infection with VSV and HSV-1 was markedly weaker in fibroblasts from the patients than in those from controls (Fig. 3, A and B). Six hours after VSV infection, viral replication rates were higher in P1 cells—as in Stat-1–deficient (*23*) and UNC-93B–deficient (*9*) cells—than in controls (Fig. 3C). Cell survival was also markedly lower for the patients than the controls and was similar to that for UNC-93B– and Stat-1–deficient cells after 24 hours of VSV and 96 hours of HSV-1 infection (Fig. 3D). Treatment with IFN-α or IFN-β complemented the phenotype of TLR3- and UNC-93B–deficient, but not Stat-1–deficient, cells (Fig. 3, C and E) in a dose-dependent manner (fig. S3). IFN-λ also partially complemented the phenotype, albeit less effectively than IFN-α or IFN-β (Fig. 3E). Our results thus demonstrate a causal relationship between heterozygosity for the P544S TLR3 mutation, impaired TLR3 signaling, abnormally weak IFN-α/β and -λ production, enhanced viral replication, and higher levels of fibroblast cell death upon viral infection.

Impaired response to poly(I:C) stimulation in MDDCs, NK, and CD8 T cells. Monocyte-derived dendritic cells (MDDCs) (*24*) from P1 and the third sibling of P2 (S3-P2), both heterozygous for the TLR3 mutation, responded more weakly than

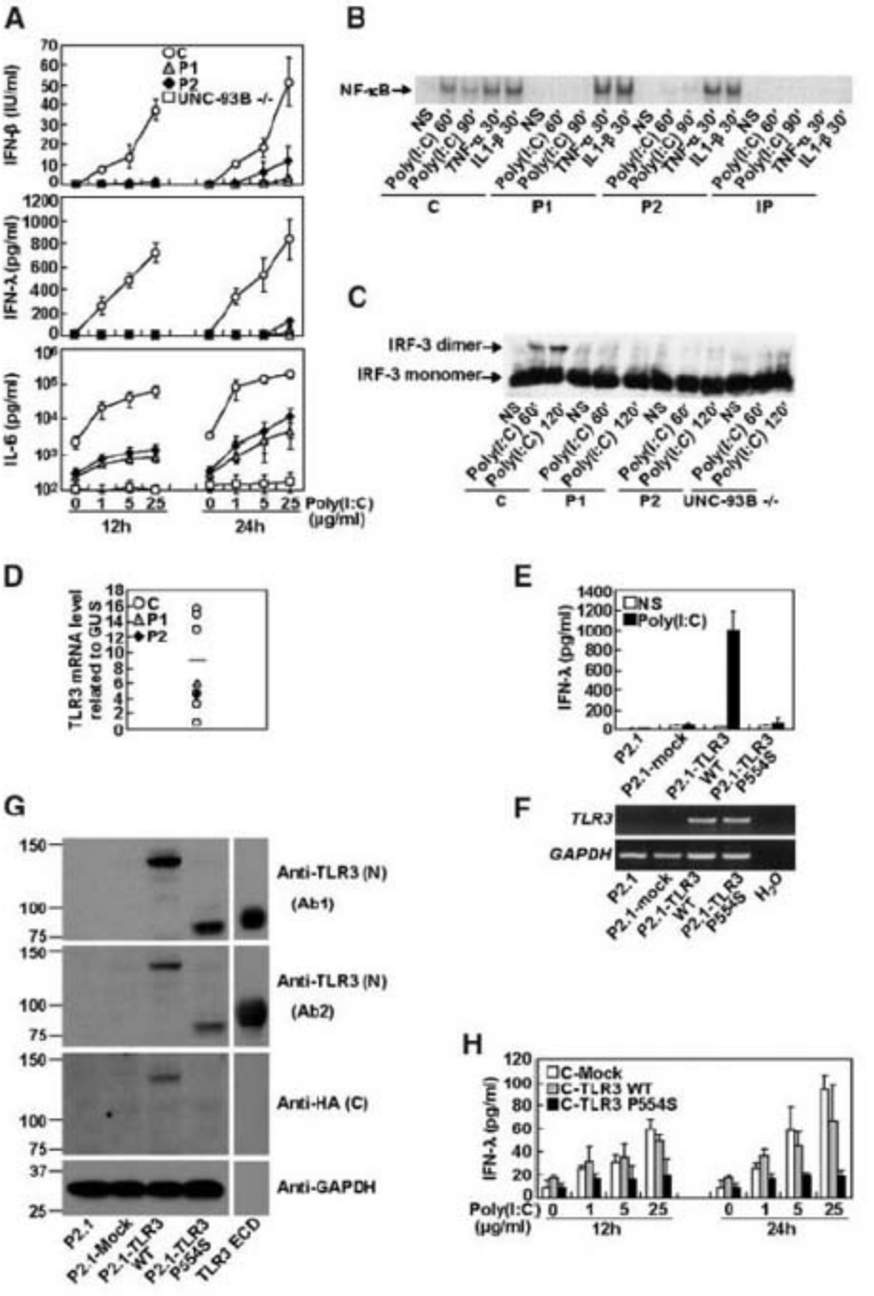

Fig. 2. Impaired response to poly(I:C) of fibroblasts and dominant-negative effect of the *TLR3* P554S allele in fibroblasts (**A**) IFN-β, -λ, and IL-6 production in SV40-transformed fibroblasts (SV40 fibroblasts) from a control (C), P1, P2, and a UNC-93B–deficient (UNC-93B$^{-/-}$) patient upon stimulation with various doses of poly(I:C) for 12 or 24 hours. (**B**) NF-κB-DNA–binding activity of nuclear extracts from the SV40 fibroblasts of a control (C), P1, P2, and a NEMO-deficient (IP) patient upon TNF-α and IL-1β stimulation for 30 min, or poly(I:C) stimulation for 60 min or 90 min, as assessed by electrophoretic mobility shift assay. The experiment is representative of two. (**C**) IRF-3 monomers and dimers in total cell extracts from SV40 fibroblasts of a control (C), P1, P2, and a UNC-93B$^{-/-}$ patient, upon poly(I:C) stimulation for 1 or 2 hours, as assessed by Western blotting. (**D**) *TLR3* mRNA levels in SV40 fibroblasts from six controls (C) [mean value indicated by (–)], P1, and P2; β-glucuronidase (GUS) was used for normalization. The experiment shown is representative of two. (**E** to **G**) In P2.1 cell lines not transfected (P2.1) or stably transfected with pUNO expression vectors carrying no insert (P2.1-mock), or the C-terminal HA-tagged *TLR3* cDNA with the WT sequence (P2.1-TLR3 WT) or with the P554S mutation (P2.1-TLR3 P554S), IFN-λ production (E) was measured after 24 hours stimulation with poly(I:C). The *TLR3* cDNA in these cells (F) is shown, with the internal amplification control *GAPDH*; the experiment shown is representative of three. TLR3 expression in these cells (G) was assessed by Western blotting, using two antibodies to N-terminal TLR3 [anti-TLR3 (N) Ab1 and anti-TLR3 (N) Ab2] and an antibody to C-terminal–tagged HA. The experiment shown is representative of six. The recombinant TLR3 ECD protein was used as a positive control for the antibody. The internal expression control was glyceraldehyde-phosphate dehydrogenase (GAPDH). (**H**) IFN-λ production, in a control SV40-fibroblast cell line, stably transfected with an empty vector (C-mock), a C-terminal HA-tagged pUNO-TLR3 WT vector (C-TLR3 WT), or an HA-tagged pUNO-TLR3 vector containing the P554S mutation (C-TLR3 P554S) upon stimulation with various doses of poly(I:C) for 12 or 24 hours. In (A), (E) and (H), the production of IFNs and IL-6 was measured by enzyme-linked immunosorbent assay (ELISA). Mean values ±SD were calculated from three independent experiments.

control cells to poly(I:C) but responded normally to LPS and R-848 in terms of IFN-β, IFN-λ, and IL-12p40 production (Fig. 4A) and CD40, CD80, and CD86 up-regulation (fig. S4A). We tested leukocyte subsets ex vivo to gain further insight into HSE pathogenesis. Unlike purified natural killer (NK) cells from controls (*25*), the patients' NK cells barely responded to poly(I:C) (Fig. 4B) but responded normally to K562 (Fig. 4B and SOM Text, note 4). Nevertheless, the known patients with inherited NK deficiency were not prone to HSE (*9*, *26*). We did not test γ/δ T cells, but unlike CD8 α/β T cells (*27*) from controls, cells from P2 and her father, both heterozygous for the P554S mutation, responded weakly to poly(I:C) costimulation (fig. S4C) but normally to costimulation with CD28 (fig. S4C). However, the known CD8- and HLA-I–deficient patients did not present HSE (*28*). Although affected by the TLR3 mutation, the contribution of NK and CD8 T cells to the pathogenesis of HSE in TLR3-heterozygous children is probably modest.

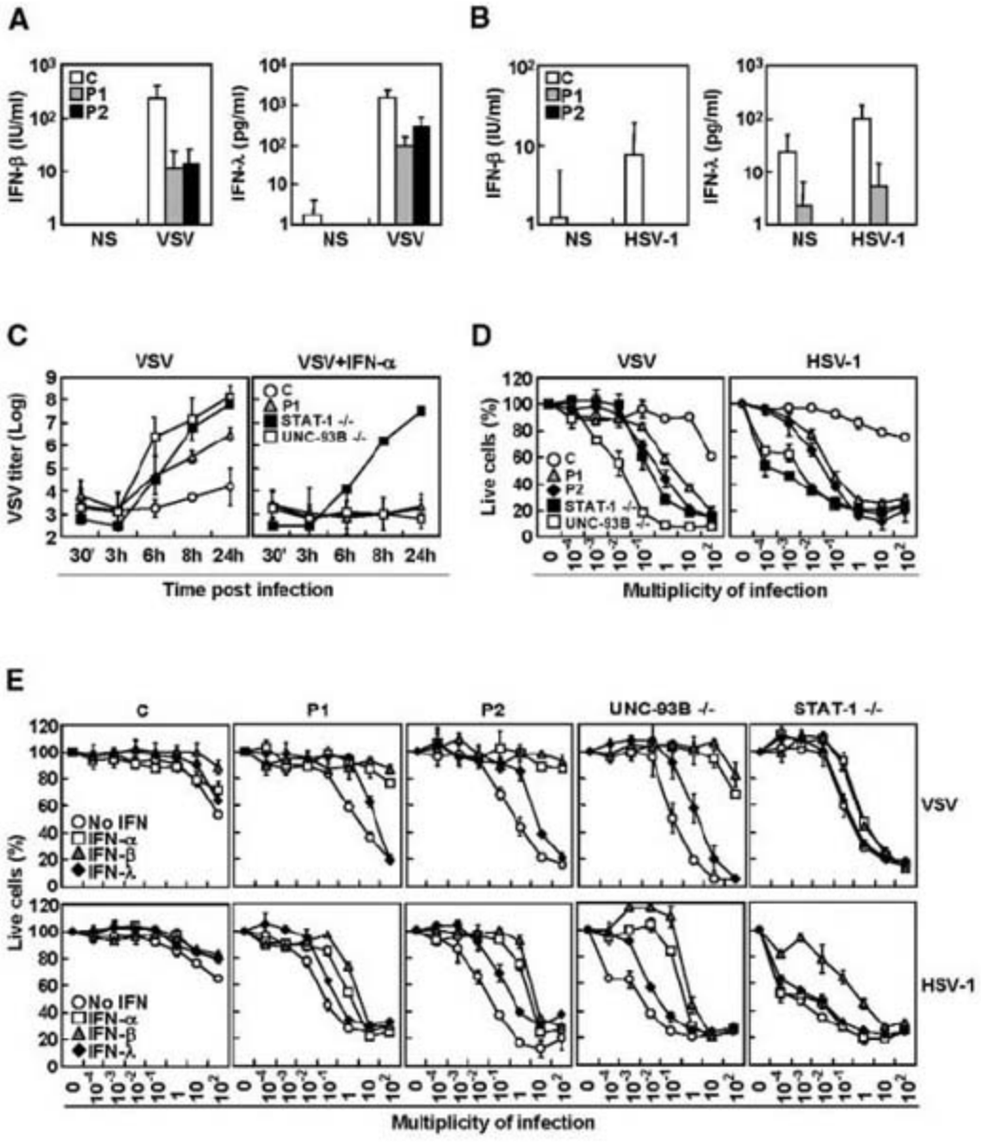

Fig. 3. High levels of viral replication and cell mortality in fibroblasts from the patients and rescue by treatment with IFN-α, -β, -λ. (**A** and **B**) IFN-β and -λ production, measured by ELISA, by SV40 fibroblasts from controls (C), P1, and P2 after 24 hours of VSV (A) or HSV-1 (B) stimulation. Mean values ±SD were calculated from six independent experiments with three different controls. (**C**) VSV titers, estimated on Vero cells, in SV40 fibroblasts from healthy controls (C), P1, a UNC-93B$^{-/-}$ patient, and a Stat1-deficient (Stat1$^{-/-}$) patient, at various times after VSV infection with or without 18 hours of pretreatment with IFN-α. Mean values ±SD of two independent experiments with two different controls are shown. (**D** and **E**) Live cell percentages, estimated by resazurin oxidation/reduction, for SV40 fibroblasts from a healthy control (C), P1, P2, a UNC-93B$^{-/-}$, and a Stat-1$^{-/-}$ patient, 24 and 96 hours after infection with various multiplicities of infection of VSV and HSV-1. The cells either were not treated (D), or were subjected to pretreatment (E) for 18 hours with recombinant IFN-α, -β or -λ and with IFN-α, -β or -λ present during infection. Mean values ±SD were calculated for three replicates in each experiment; one representative of three experiments with two different controls is shown.

Response of blood DCs and keratinocytes to poly(I:C) stimulation. Like IRAK-4– and UNC-93B–deficient peripheral blood mononuclear cells (PBMCs) (*7*, *9*), the patients' cells responded normally to poly(I:C) in terms of IFN-α, -β and -λ production (fig. S1, A to C, and fig. S5A). The patients' purified myeloid DCs (MDCs) (*24*) responded normally to poly(I:C) in terms of IFN-λ production (Fig. 4C). Moreover, IFN-α (Fig. 4D) and -λ (fig. S5B) were produced by poly(I:C)-stimulated purified plasmacytoid DCs (PDCs) from patients and controls, although PDCs are not thought to express TLR3 (*24*). The lack of clinical HSV-1 dissemination, particularly by the blood, in patients with HSE may therefore be due to the induction of IFNs by MDCs and PDCs stimulated with dsRNA or other viral intermediates (*29*). HSV-1 also does not spread to epithelia during or following HSE (*9*). Several epithelial cell types, keratinocytes in particular (*30*), express TLR3 and respond to poly(I:C). TLR3-heterozygous keratinocytes from P2 did not respond to poly(I:C), as shown by measurements of IL-6 secretion (Fig. 4E). However, they responded to poly(I:C), as shown by IFN-λ (Fig. 4E) and IL-8 (fig. S5C) production. The IFN-λ response of the patients' keratinocytes suggested that the sensing of dsRNA and, possibly, other viral intermediates (*29*) in epithelial cells prevented the epithelial dissemination of HSV-1 in TLR3-heterozygous patients with HSE. The poly(I:C) responsiveness of DCs and keratinocytes probably operated through TLR3-independent pathways (*29*), although we cannot exclude the possibility of residual TLR3 signaling or a lack of dominance of the P554S TLR3 mutant in such cells.

Most viruses trigger IFNs in TLR3 heterozygous cells. The lack of other severe viral diseases in TLR3-heterozygous and UNC-93B–deficient patients with HSE is intriguing (*9*, *31*). Our demonstration of poly(I:C) responsiveness in keratinocytes and blood DCs is important because most viruses enter the host via the epithelium, and most forms of human viral encephalitis other than HSE and rabies are blood-borne. We then stimulated the patients' blood cells with 11 viruses (*7*, *9*). TLR3-deficient PBMCs displayed normal production of IFN-α, -β and -λ, and other cytokines in response to the viruses tested (Fig. 4F and fig. S5D). Similarly, cells from IRAK-4–deficient patients showed normal or weak but detectable responses to all viruses (*7*). Cells from UNC-93B–deficient patients showed impaired, but not abolished, responses to several viruses, including HSV-1 (*9*). We then tested the responses of the patients' fibroblasts to the six viruses that stimulated IFN-β and -λ production in control fibroblasts. Like IRAK-4–deficient fibroblasts (*7*), both TLR3-deficient and UNC93-B–deficient fibroblasts responded well to four of the viruses, but unlike the IRAK-4–deficient fibroblasts (*7*), they responded poorly to HSV-1 and VSV (Fig. 4G). The in-

duction of IFN-α, -β, and -λ in blood cells and fibroblasts from TLR3-heterozygous patients, after stimulation with most of the viruses tested, was consistent with the natural resistance of these patients to most viruses other than HSV-1.

Concluding remarks. After autosomal recessive UNC-93B deficiency (*9*), autosomal dominant TLR3 deficiency is the second genetic etiology of isolated HSE to be identified. Because Stat-1–deficient (*32*) patients are also prone to HSE (and other infectious diseases), the molecular pathogenesis of HSE primarily involves impaired TLR3-dependent, IFN-α, -β, and -λ responses. Several lines of evidence also indicate that the pathogenic cellular mechanism underlying HSE in TLR3-heterozygous patients involves an intrinsic defect affecting CNS-resident cells: the neurotropic infection of the CNS by HSV-1, the CNS-restricted clinical course of HSE, the widespread and preferential expression of TLR3 in the CNS, the poly(I:C)–inducible production of antiviral IFNs by blood DCs in TLR3 heterozygotes, and the absence of HSE in patients with conventional primary immunodeficiencies. In addition to revealing the pathogenic mechanism and a basis for both molecular diagnosis and genetic counseling, our findings provide further support for the treatment of HSE patients with IFN-α in addition to acyclovir (*9*). Interestingly, five of the seven TLR3-deficient individuals and one of the three UNC-93B–deficient individuals did not develop HSE after HSV-1 infection. The incomplete clinical penetrance of TLR3 and UNC-93B deficiency is consistent with the typically sporadic, as opposed to familial, occurrence of HSE (*8*, *9*). Multiple factors may affect clinical penetrance, including age at infection with HSV-1, the viral inoculum, and human modifier genes.

The infection of TLR3-deficient mice with HSV-1 has not yet been reported, but mouse TLR3 appears to be largely redundant in antiviral immunity. TLR3-deficient mice are susceptible to encephalomyocarditis virus (EMCV) (*33*) and mouse cytomegalovirus (MCMV) (*34*, *35*), at least in some experimental conditions and, to a lesser extent, to respiratory syncytial virus (RSV) (*36*). However, TLR3-deficient mice have normal resistance to lymphocytic choriomeningitis virus

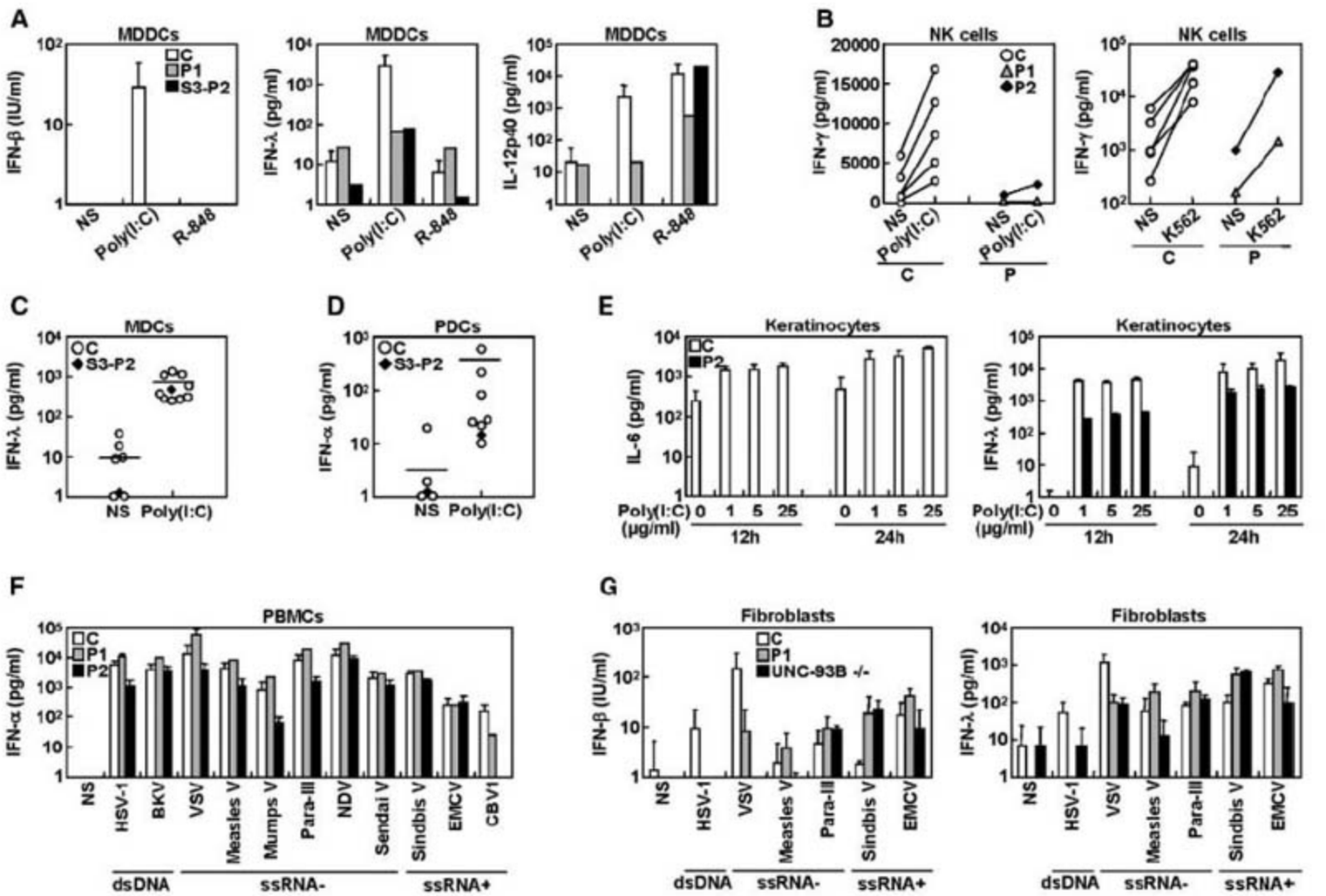

Fig. 4. Impaired response to poly(I:C) in MDDCs and NK cells but not in blood DCs and keratinocytes; most viruses trigger IFNs in TLR3 heterozygous blood and fibroblasts (**A**) IFN-β, -λ, and IL-12p40 production, by MDDCs from controls (C), P1, and a sister of P2 (S3-P2) heterozygous for the P554S mutation. Mean values ±SD were calculated from the data for 12 controls. (**B**) IFN-γ production, in purified NK cells from five controls (C), P1, and P2, upon stimulation with poly(I:C) or K562 for 24 hours in the presence of IL-12. (**C**) IFN-λ production in MDCs from eight controls (C) [mean value indicated by (—)] and a sister of P2 (S3-P2) heterozygous for the P554S mutation. (**D**) IFN-α production, in PDCs from seven controls (C) [mean value indicated by (—)] and S3-P2. (**E**) IL-6 and IFN-λ production by keratinocytes from controls (C) and P2. Mean values ±SD were calculated for two replicates in each experiment, with two different controls. (**F**) IFN-α production by PBMCs 24 hours after stimulation with intact viruses. Means ±SD were calculated for the controls (C) from data for six healthy individuals, each tested once, for P1 (tested four times for HSV-1 and VSV and once for the other viruses), and for P2 (tested twice for all the viruses). (**G**) IFN-β and -λ production, 24 hours after stimulation with intact viruses, in fibroblasts from controls, P1, and a UNC-93B$^{-/-}$ patient. Mean values ±SD were calculated from three independent experiments with two different controls. The production of IFNs and IL-6 was measured by ELISA in (A) to (G).

(LCMV), VSV, and reovirus (*35*). Moreover, TLR3-deficient mice are resistant to influenza A virus (*37*), West Nile virus (*38*), and phlebovirus (*39*). Human TLR3 also appears to be largely redundant for antiviral immunity, as the known TLR3- and UNC-93B–deficient patients have had infections with numerous viruses without developing severe disease (*9*, *31*). Nevertheless, human TLR3 is essential for primary immunity to HSV-1 in the CNS, at least in some circumstances. Our study provides conclusive evidence that an individual TLR can play a nonredundant role in host defense in the setting of a natural ecosystem. Given its ability to recognize dsRNA, human TLR3 may have been of evolutionary importance: Most patients with HSE died until the advent of acyclovir in 1981 (*8*). As naturally occurring mutations in TLR3 may be dominant negative, it is tempting to speculate that HSV-1 and other neurotropic viruses may have exerted direct selective pressure, driving the maintenance of human TLR3.

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Materials and Methods
SOM Text
Figs. S1 to S5
References

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REPORTS

Lighting the Universe with Filaments

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The first stars in the universe form when chemically pristine gas heats as it falls into dark-matter potential wells, cools radiatively because of the formation of molecular hydrogen, and becomes self-gravitating. Using supercomputer simulations, we demonstrated that the stars' properties depend critically on the currently unknown nature of the dark matter. If the dark-matter particles have intrinsic velocities that wipe out small-scale structure, then the first stars form in filaments with lengths on the order of the free-streaming scale, which can be ~10^{20} meters (~3 kiloparsecs, corresponding to a baryonic mass of ~10^7 solar masses) for realistic "warm dark matter" candidates. Fragmentation of the filaments forms stars with a range of masses, which may explain the observed peculiar element abundance pattern of extremely metal-poor stars, whereas coalescence of fragments and stars during the filament's ultimate collapse may seed the supermassive black holes that lurk in the centers of most massive galaxies.

Most of the matter in the universe does not interact with light except gravitationally. This "dark matter" is usually assumed to be "cold," meaning that its velocity dispersion is sufficiently small for density perturbations imprinted in the early universe to persist up to very small scales. Although this model is able to describe the large-scale distribution of galaxies in impressive detail, it may face problems on the scale of galaxies and below; for example, it may predict too many satellite galaxies (*1*), as well as too-cuspy profiles for the dark-matter halos that surround galaxies (*2*).

Dark matter has yet to be detected in the laboratory, however, and there exist many viable dark-matter candidates from particle physics that are not cold. "Warm" dark matter (WDM) particles have intrinsic thermal velocities, and these motions quench the growth of structure below a "free-streaming" scale (the distance over which a typical WDM particle travels), which depends on the nature of the particle. Because small and dense halos do not form below the free-streaming scale, the dark-matter halos that surround galaxies in a WDM model have far less substructure and are less concentrated as compared with their cold dark matter (CDM) counterparts, which may help alleviate both the satellite and galactic-core problems (*3*). Structures on larger scales are similar in WDM and CDM, and therefore the distribution of galaxies is not affected. The first generation of stars in the universe forms when primordial gas gets compressed by falling into small–dark-matter potential wells (*4*–*7*). Because WDM affects structure formation on such small scales, it may influence how the first stars form; we have performed simulations to analyze this idea in more detail.

Large-scale power in the spectrum of density perturbations causes progenitors of present-day clusters of galaxies to be among the first objects to condense out of the initially almost smooth mass distribution. We studied the early formation stages of such an object by identifying a massive cluster of galaxies in a dark-matter simulation of a large cosmological volume at redshift $z = 0$ and used a multiscale technique (*8*, *9*) to resimulate its formation and evolution with the cosmological hydrodynamics code Gadget-2 (*9*, *10*). Baryons compressed by falling into the developing dark-matter potential wells cool radiatively through molecular hydrogen emission lines (*9*, *11*); we

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followed the formation of molecular hydrogen and its cooling using a sophisticated chemistry network (*6*). The parent simulation, from which we picked the resimulated region, followed the growth of structure in a CDM-dominated universe with a cosmological constant Λ; we performed the resimulations assuming both CDM and WDM as dark matter. In this WDM model, small-scale power in the density fluctuations is exponentially suppressed below ~100 co-moving kpc, mimicking free-streaming of gravitino particles with mass m_{WDM} = 3 keV (*3*). Gravitinos are a popular WDM candidate (*12*), but our results are insensitive to the exact choice of WDM particle as long as its free-streaming length is more than a few tens of co-moving kiloparsecs. Therefore, even if the gravitino were slightly more massive or if the WDM were instead a sterile neutrino [another popular WDM candidate (*13*)], our results would not change appreciably. Observations of the clustering of neutral gas along sight lines to distant quasars (the Lyman-α forest of absorption lines) probe scales 1 to 40 Mpc when the density perturbations on these scales are still small, and the presence or absence of substantial substructure in these observations can constrain the masses of WDM particles (*14*, *15*); our choice of WDM particle mass (3 keV; the corresponding mass scale is ~3 × 10^8 $M_\odot$, where $M_\odot$ is the solar mass) is well above this lower limit (~2 keV) (*14*, *15*). The initial amplitude of the imposed density perturbations in our simulations is normalized to the level seen in the cosmic microwave background radiation (*16*), and our simulations start at redshift z ~200. (See the supporting online material for more details on these simulations.)

The growth of structure in these resimulations leads to a pattern of filaments and sheets (Fig. 1) that is familiar from the local large-scale distribution of galaxies. This is because the assumed Gaussian spectrum of density perturbations, appropriate for an inflationary model, leads to collapse along one (sheet) and two (filament) directions before the formation of halos. Although the large-scale filamentary pattern is very similar in CDM and WDM, the structure of the filaments themselves is very different. Whereas the CDM filaments fragment into numerous nearly spherical high-density regions ("halos") (Fig. 1A), the WDM filaments are mostly devoid of such substructure (Fig. 1B). Figure 1, C and D, depicts the WDM filament at an earlier time before any of the other filaments have formed: The central density is very high (hydrogen number density $n_h \sim 10^4$ cm$^{-3} \approx 10^6 \langle n_h \rangle$) but no dark-matter halo has formed yet. It is well known that the Poisson noise in simulation codes that use particles to represent the dark matter leads to spurious fragmentation of the filaments that form in such WDM simulations (*17*, *18*). We therefore ended the analysis of our WDM simulations well before the filaments fragmented.

The length L of the filament (~3 kpc) is on the order of the imposed WDM free-streaming scale, as expected: $L \sim 4$ kpc at redshift $z = 23.34$ when the universe is 140 million years old. Gas and dark matter accrete perpendicular onto the filament's axis (Fig. 2). Dark-matter particles falling into the filament perform damped oscillations as the potential well deepens. At $r \sim 50$ pc (where r is the distance perpendicular to the filament's axis), dark-matter particles falling into the well encounter particles that fell in from the other side, and these successive instances of "orbit crossing" give rise to the steps in the density seen in Fig. 1B. Baryons do not undergo orbit crossing but the gas gets compressed to a temperature $T \approx 7000$ K at $r \sim 20$ pc. Rapid buildup of H_2 induces cooling, and the gas starts to dominate the matter density further downstream so that the ratio of gas to dark-matter densities is $\rho_b/\rho_{DM} \sim 15 = 100\langle\rho_b\rangle/\langle\rho_{DM}\rangle$ at $r = 2$ pc. At $r < 2$ pc where the gas dominates, the ratios of principal axes of the filament are $b/a = 0.123$ and $c/a = 0.118$; hence, the filament is very nearly cylindrical. The properties of both the gas and the dark matter are very uniform along the whole length of the filament. The cylindrical density profile below 10 pc is approximately $\rho \propto r^{-2.8}$ for $2 \leq r \leq 8$ pc and $\rho \propto r^{-2}$ for $r < 2$ pc. This is in contrast to $\rho \propto r^{-2.3}$ for the spherically averaged profile of the gas in CDM halos on a comparable scale (*6*, *7*). The central H_2 abundance reaches 10^{-3}, higher than in the CDM case because of the higher temperature reached behind the accretion shock. This higher temperature and the associated higher ionization fraction will also enhance the importance of deuterated molecular hydrogen (HD) cooling at later stages (*19*, *20*).

The nonlinear collapse into a thin filament found in these WDM simulations is in sharp contrast to what happens in the CDM case. There the first objects to reach high densities are discrete, nearly spherical dark-matter halos (gravitationally bound concentrations of dark matter) that form at tiny masses and build up hierarchically through mergers and accretion. Some halos have a sufficiently deep potential well to accrete and shock baryons, enabling H_2 formation and radiative cooling. Runaway collapse of the rapidly accreting self-gravitating gas is thought to lead to the formation of a single massive star per cooling

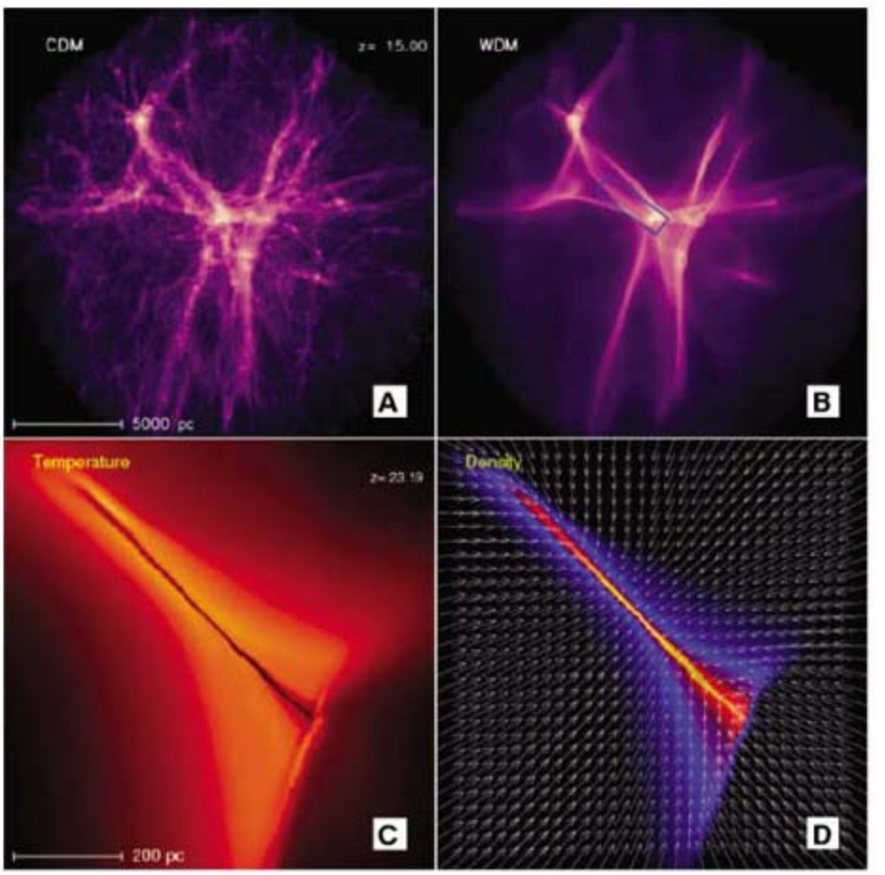

Fig. 1. (**A** and **B**) Dark-matter density structure of the progenitor of a redshift $z = 0$ massive cluster of galaxies at $z = 15$ when the thermal velocities of the dark-matter particles are negligible (CDM) (A) and when the dark matter is warm (a gravitino with $m_{WDM} = 3$ keV) (B). Although both models produce a characteristic filamentary pattern in the density, the CDM filaments fragment into numerous nearly spherical halos, whereas free-streaming of the WDM prevents this type of substructure from forming. (**C** and **D**) Gas temperature (C) and density (D) in the WDM filament, indicated by the blue box in (B), at an earlier redshift ($z = 23.34$) when only this filament had formed. Gas accretes very uniformly onto the filament, as indicated by the velocity vectors, and heats as it gets compressed but cools further downstream because of the formation of H_2, making the center of the filament cold and dense. The filament shown here is almost perfectly cylindrical; usually they are elliptical in shape.

halo (*4*, *6*, *7*). The absence of small-scale power in WDM prevents halos from forming before the filament itself becomes highly nonlinear. Although our resimulations focus on the progenitor of a massive cluster, and hence the forming object collapses unusually early on, the fact that very high densities are reached in a filament, as opposed to a spherical halo, is generic to WDM.

The stability of collapsing filamentary clouds has been investigated in the context of the formation of cloud cores, for example in (*21*, *22*), and applied to early-universe filaments (*23*). The inability of gas to cool sufficiently fast usually limits the collapse time of the filament by the cooling time, $t_d \equiv \rho/\dot{\rho} \sim t_c \equiv nk_BT/\Lambda$ (where t_d is the dynamical time, t_c is the cooling time, n is the density, k_B is the Boltzmann constant, T is the temperature, and Λ is the cooling rate due to H_2 and HD cooling). Perturbations start growing, possibly leading to fragmentation, when $t_d >> t_p$, where t_p is the inverse growth rate of perturbations. If the gas cooling is efficient, $t_d \sim t_c << t_p$, and perturbations do not grow. At $n = n_1 \sim 10^5$ cm^{-3}, the level population of H_2 reaches local thermodynamic equilibrium, making $\Lambda \propto n$ instead of $\propto n^2$, and t_c becomes independent of density (*11*). A sufficiently massive filament may yet survive fragmentation at this stage, and at higher density $n \sim 10^9$ cm^{-3}, three-body processes promote the formation of H_2 and the cooling time decreases again. However, when $n \geq n_2 = 10^{12}$ cm^{-3} the gas becomes optically thick in the H_2 cooling transitions, slowing the collapse, and the filament is once more in danger of fragmenting. Collision-induced continuum emission will again decrease the cooling time when $n \sim 10^{14}$ cm^{-3}, until the gas becomes optically thick also to this cooling radiation at densities $n \geq n_3 = 10^{16}$ cm^{-3} (*20*, *24*). The physics of the H_2 molecule therefore sets three densities at which the filament may fragment. The typical fragment masses are on the order of tens of solar masses, solar masses, and subsolar masses for fragmentation at densities n_1, n_2, and n_3, respectively (*23*).

The tidal field around the filament breaks the cylindrical symmetry on scales comparable to the filament's length (Fig. 1) and can trigger the gas dynamical instabilities that ultimately lead to fragmentation. Unfortunately, our current simulations are not able to follow this process in detail because these tiny deviations from symmetry are overpowered by numerical noise caused by the graininess of the particle distribution. This causes the filament to fragment very rapidly as expected, yet the scale of the fragmentation is artificial. In the WDM universe, the small-scale perturbations that trigger fragmentation in the simulations are not present and need to be generated through the transfer of power from larger scales. Because this is a relatively slow process, the central density will have reached the higher value n_2 or even higher, implying small fragment masses on the order of a solar mass or below. Such fragments can coalesce to form more massive clumps, as has been demonstrated in two-dimensional numerical simulations (*22*). Even if individual cores survive, they may still grow in mass through accretion.

Detailed observations of star-forming clouds in the Milky Way reveal that the low-mass stellar mass function is very similar to that of the dense prestellar cloud cores within the ambient cloud, although it is not yet clear what determines the cut-off at high masses. This close similarity might indicate that the process of cloud fragmentation plays an important role in determining the initial mass function (*25*). If this also applies to star-formation in a WDM filament, then it is plausible that fragmentation will lead to a burst of star formation that includes low-mass stars with masses ~1 $M_\odot$ or below but also much more massive stars built through mergers and accretion. The more massive stars will end their short lives through supernova explosions or collapse to form intermediate-mass black holes, and some of the very-low-mass stars may potentially survive until today. Although the details of this scenario are uncertain, it is clear that the stellar mass function will be quite different from the CDM case.

The low-mass Milky Way stars discovered in the Hamburg/European Southern Observatory survey HE 0107-5240 (*26*) and HE 1327-2326 (*27*) have extremely low metallicities (*28*) of [Fe/H] ~ −5 and peculiar element abundances, for example [C/Fe] > 1. An initial mass function of

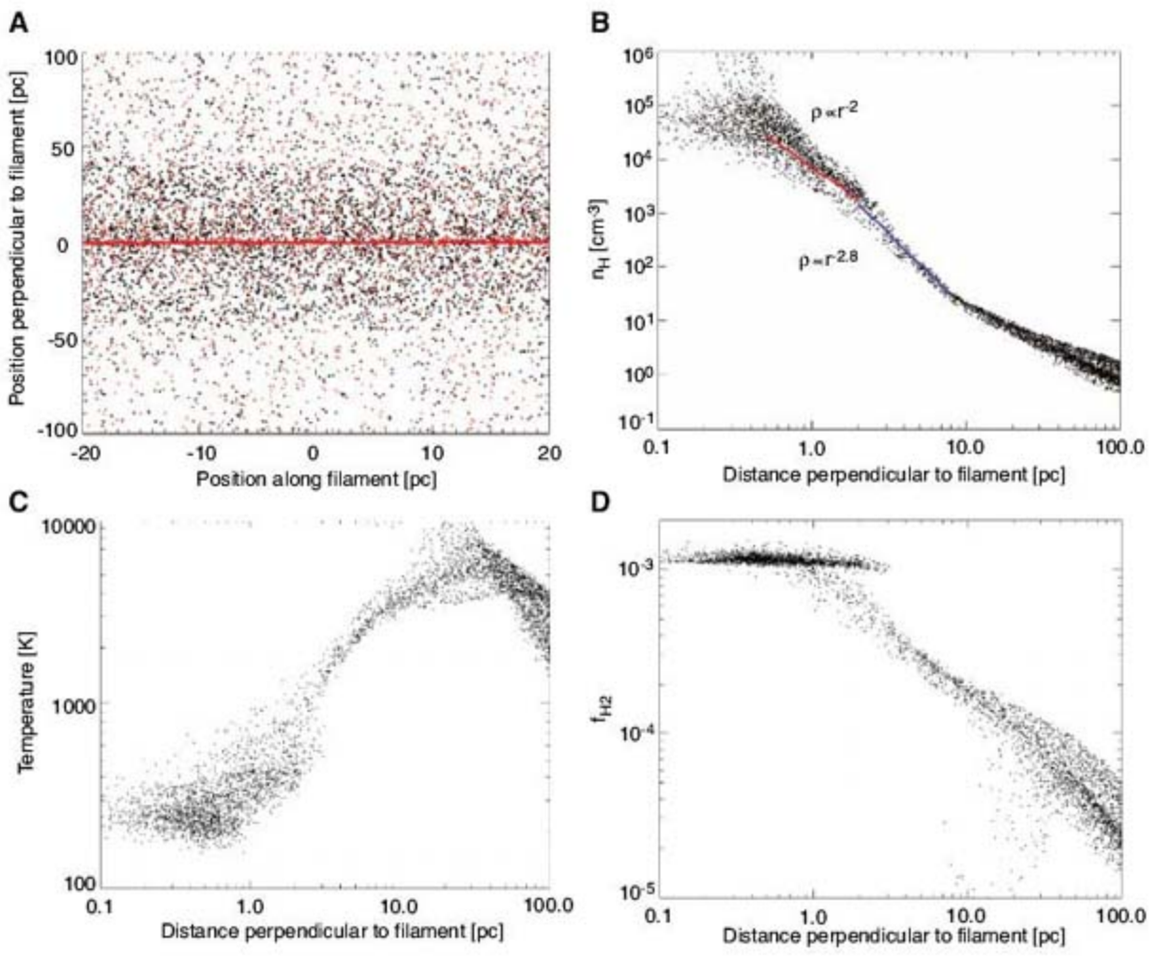

Fig. 2. Gas and dark-matter profiles of the WDM filament shown in Fig. 1, C and D. (**A**) Accretion of dark-matter particles (black) and gas particles (red); the horizontal and vertical scales are different (along and perpendicular to the filament, respectively). The dark matter undergoes orbit crossing (multivalued velocities) at $r \sim 50$ pc, whereas the gas gets shocked much closer in (~20 pc) and dominates further downstream. (**B**) Gas density profile, as measured perpendicular to the filament's axis. Lines $\rho \propto r^{-2}$ and $\rho \propto r^{-2.8}$ serve to guide the eye. (**C**) Temperature profile. Gas heats as it gets compressed, but the rapid buildup of H_2 cools the gas further in. (**D**) Buildup of molecular hydrogen fraction, f_{H2}, during the accretion.

zero-metallicity first stars with a range of masses, as we suggested might be the case in WDM, could explain these stars either as due to self-pollution or pre-enrichment by intermediate-mass (tens of solar masses) supernovae (*29*). Such first-generation low- and intermediate-mass stars are not thought to form in CDM (*4*, *6*, *7*). Therefore, although the present observational evidence is not yet unambiguous, a future detection of zero-metallicity low-mass first stars may indicate that the dark matter is warm.

Free-streaming of the WDM considerably decreases the number density of halos that host early-star formation, which could delay reionization as compared with CDM (*30*). However, the additional mode of star formation in filaments could partly compensate, making it unclear whether reionization is indeed delayed when the dark matter is warm.

What is the ultimate fate of such $\sim 10^7\ M_\odot$ filaments? Eventually the filament will collapse along its long axis, and because its mean density is very high, a large number of collisions between cloud cores and stars would appear inevitable. Such collisions could build up a massive object that can seed the formation of the supermassive black holes that power redshift $z \sim 6$ quasars and appear to lurk in the centers of most large galaxies today.

The different outcome of WDM versus CDM is because the thermal velocities of the WDM particles prevent halos from forming before the filaments themselves form stars. This happens when the free-streaming length introduced by the dark matter's thermal velocities is more than a few tens of co-moving kiloparsecs so that the filaments are sufficiently massive to heat infalling gas to more than ~1000 K, enabling efficient cooling by molecular hydrogen. If we simulate a WDM universe with a much shorter free-streaming length (for example, ~20 kpc corresponding to a gravitino mass $m_{\mathrm{WDM}} = 15$ keV), star formation proceeds in a similar way to the CDM case, in good agreement with earlier work (*31*). The likely very different initial mass function of the first stars and the rapid formation of massive black holes in a WDM scenario with $m_{\mathrm{WDM}} \sim 3$ keV, as opposed to CDM, implies a very different early thermal- and metal-enrichment history of the universe, greatly affecting subsequent galaxy formation. It appears, therefore, that the way in which quasar, star, and galaxy formation started depends strongly on the nature of the dark matter.

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SOM Text
Figs. S1 to S3
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Phase-Coherent Transport in Graphene Quantum Billiards

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As an emergent electronic material and model system for condensed-matter physics, graphene and its electrical transport properties have become a subject of intense focus. By performing low-temperature transport spectroscopy on single-layer and bilayer graphene, we observe ballistic propagation and quantum interference of multiply reflected waves of charges from normal electrodes and multiple Andreev reflections from superconducting electrodes, thereby realizing quantum billiards in which scattering only occurs at the boundaries. In contrast to the conductivity of conventional two-dimensional materials, graphene's conductivity at the Dirac point is geometry-dependent because of conduction via evanescent modes, approaching the theoretical value $4e^2/\pi h$ (where e is the electron charge and h is Planck's constant) only for short and wide devices. These distinctive transport properties have important implications for understanding chaotic quantum systems and implementing nanoelectronic devices, such as ballistic transistors.

Graphene is a two-dimensional (2D) honeycomb lattice of carbon atoms and exhibits an energy dispersion relation in which the low-lying excitations behave like massless relativistic Dirac fermions (*1*–*3*), and a graphene bilayer's band structure resembles a zero band-gap semiconductor (Fig. 1A). This band structure is predicted to give rise to several unconventional phenomena, such as the Klein paradox (*4*) (i.e., the ability of relativistic particles to tunnel through high barriers with perfect transmission) and the Vaselago lensing effect (*5*) (i.e., focusing of charges in a *p-n* junction). Technologically, graphene is an attractive material for nanoscale electronics engineering. As a 2D relative of carbon nanotubes, it has superior mobility, current-carrying capacity, and thermal conductivity; but in contrast to nanotubes, lithographic techniques can be used in graphene for device synthesis and tailoring transport properties (*6*), thus expediting integration with

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silicon-based complementary metal-oxide semiconductor technology. In the long term, graphene's unusual properties could enable new functionality in nanoelectronics.

Many of the proposed phenomena and devices assume ballistic charge propagation in conjunction with graphene's distinctive band structure. Yet, a clear demonstration of the ballistic transport regime in graphene has been lacking, whereas the exact electrical conductivity at the Dirac point, σ_{min}, has been the focus of many recent theoretical works [see (*4*) for a review]. We experimentally explore σ_{min} in both diffusive and ballistic regimes for single-layer graphene (SLG) and bilayer graphene (BLG) and establish ballistic and phase-coherent transport in short devices coupled to normal and superconducting electrodes. These graphene quantum billiards are expected to reveal unexpected features in spectra statistics in massless Dirac fermion billiards (*7*) and in Andreev billiards (*8*) (i.e., billiards with superconducting boundaries), thus enabling differentiation between chaotic and integrable dynamics and providing insight into quantum chaos. In addition to realizing graphene electron or hole resonators, specular Andreev reflection (*9*, *10*) in Andreev billiards can be exploited for chargeless transport of pure spin (*11*) and thermopower (*12*) currents.

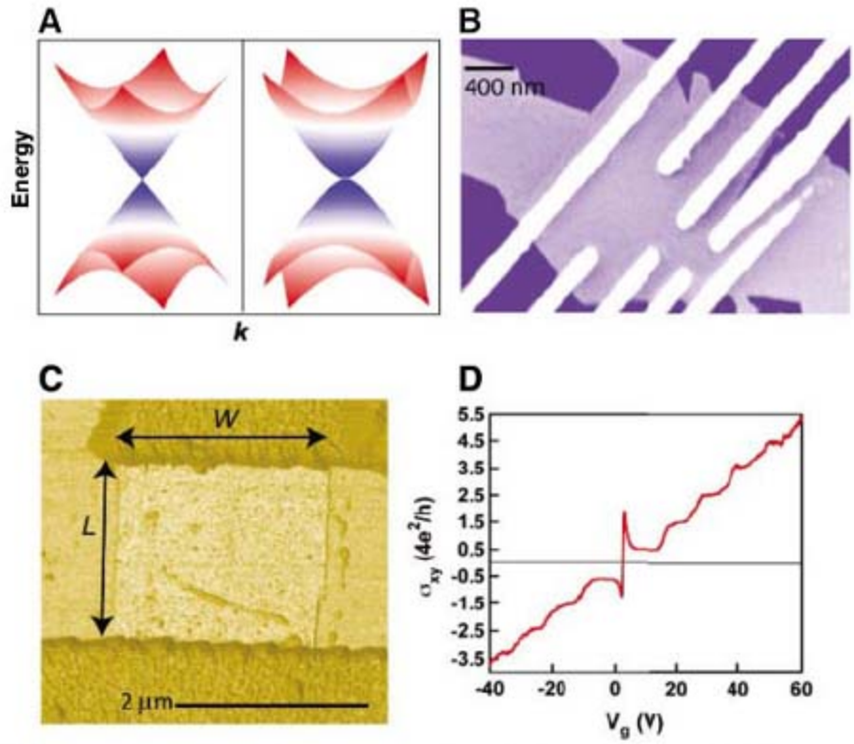

Fig. 1. (**A**) Energy dispersion relations for SLG (left panel) and BLG (right panel). k is the wave vector of charges. (**B**) Scanning electron microscope image of a SLG device in Hall-bar geometry. (**C**) Atomic force microscope image of a two-terminal device with a measured thickness of 3.5 nm, indicating the presence of several atomic layers. (**D**) SLG's σ_{xy} in units of $4e^2/h$ versus V_g at H = 8 T and 260 mK.

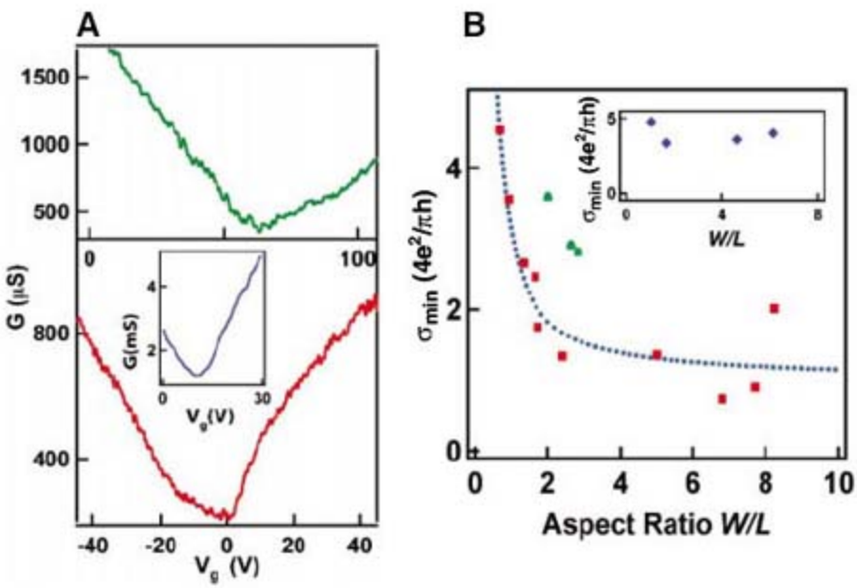

Fig. 2. (**A**) Conductance G versus V_g for small-area SLG and BLG devices (bottom and top panels, respectively). (Inset) $G(V_g)$ for a large-area SLG. (**B**) σ_{min} (in units of $4e^2/\pi h$) versus the device aspect ratio W/L. Red squares, small SLG devices; green triangles, BLG devices. The dotted line is calculated from Eq. 1. (Inset) σ_{min} versus W/L. Blue diamonds, large SLG devices.

To address the controversy, we focus on the zero-bias conductance of SLG and BLG devices as a function of V_g at an applied magnetic field H = 0 and temperature T = 1.5 K, which is above the superconducting transition temperature T_c of bulk Al. As shown in Fig. 2A, the device conductance is high at large negative and positive V_g, corresponding to highly hole- and electron-doped regimes, respectively. At the Dirac point, the device conductance reaches a minimum G_{min}, which ranges from 148 to 1200 μS for all devices studied. For devices with relatively large source-drain separation (L > ~1 μm) and large area (A > 3 μm^2), values of minimum conductivity $\sigma_{min} = (L/W)G_{min}$ of these devices are geometry-independent and relatively constant: ~3.3 to 4.7 G_0 (Fig. 2B, inset). Here, L and W are the length and width of the source-drain conduction channel, respectively. This finding is fully consistent with that in the previous report for devices with L ~ 3 to 10 μm and A > 10 μm^2 (*2*).

For "small" devices with $L < 500$ nm and $A < 0.2\ \mu m^2$, however, a qualitatively different behavior emerges: σ_{min} is no longer constant but varies from 0.8 to 4.6 G_0. Plotting measured values of σ_{min} (in units of $4e^2/\pi h$) versus the aspect ratio W/L, where data from SLG and BLG devices are represented by red squares and green triangles, respectively (Fig. 2B), we see that when $W/L < 2$, σ_{min} is ~ 2 to 4 and systematically decreases with increasing aspect ratio; for the devices with $W/L > 4$, σ_{min} is close to 1. Our results agree with recent theoretical works (*15*, *16*): In the ballistic regime, σ_{min} depends on the graphene's geometry and the microscopic details of the edges, approaching the universal value of $4e^2/\pi h$ when boundary effects are negligible, which is achieved for wide and short graphene strips with $W >> L$.

Quantitatively, at the Dirac point, the conductivity of a ballistic graphene strip with "armchair" edges is given by (*15*)

$$\sigma_{min} = G_{min}\frac{L}{W} = \frac{4e^2}{h}\frac{L}{W}\sum_{n=0}^{N-1} T_n \qquad (1)$$

where T_n is the transmission probability of the nth conductance channel, $T_n = \frac{1}{\cosh^2(\pi n L/W)}$. Using $N = 100$ (the sum converges quickly for $N > 10$, where N denotes the total number of channels), we calculate σ_{min} as a function of W/L (Fig. 2B, dotted line), in excellent agreement with the experimental data. This result suggests the electrical transport in graphene is ballistic up to lengths ~0.5 to 1 μm, which is consistent with results from QH measurements (*2*). Device 10, corresponding to the data point at $W/L = 8.25$ and $\sigma_{min} \sim 2\ G_0$, has relatively large area (~1.2 μm^2) and appears appreciably above the theoretical curve. Moreover, the bilayer devices appear to fall on a different curve, as expected from theoretical predictions (*19*–*21*).

Our experimental results provide strong evidence for two transport regimes: Small and short graphene strips exhibit ballistic transport,

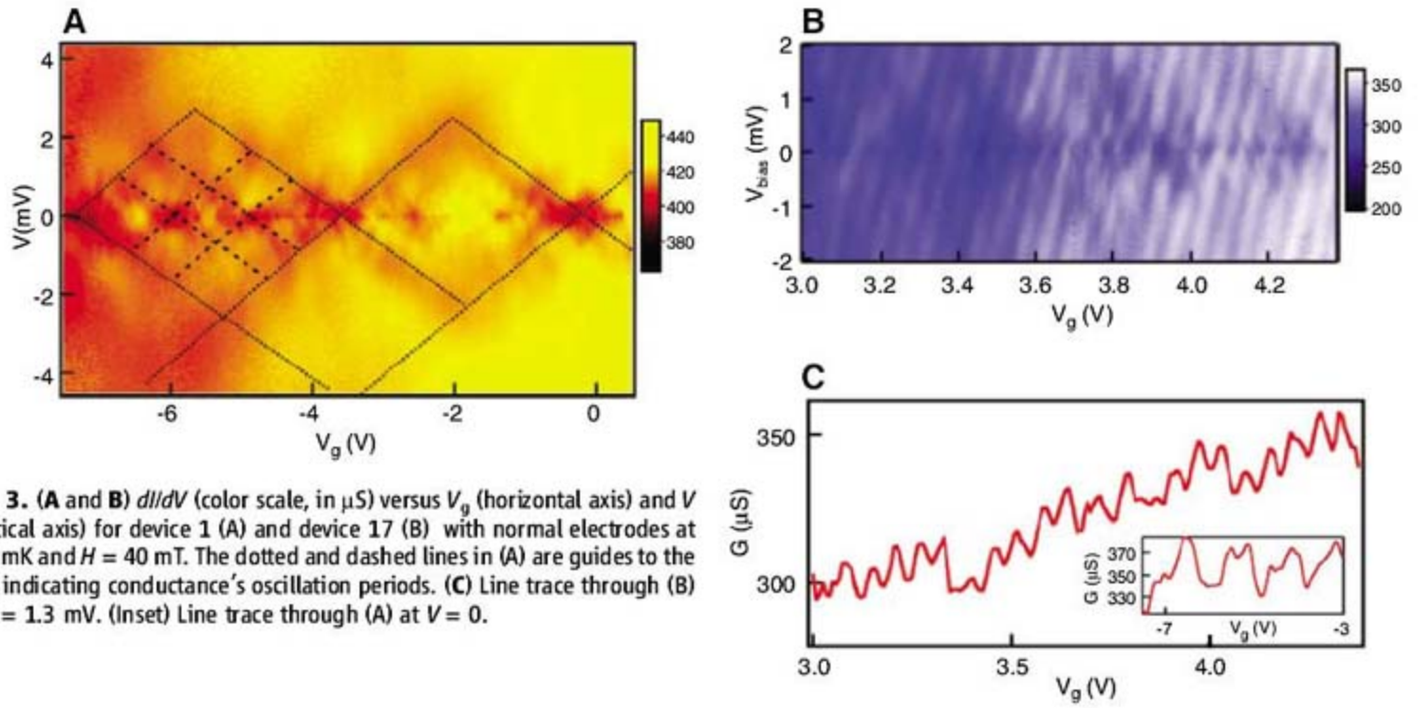

Fig. 3. (**A** and **B**) *dI/dV* (color scale, in μS) versus V_g (horizontal axis) and V (vertical axis) for device 1 (A) and device 17 (B) with normal electrodes at 260 mK and $H = 40$ mT. The dotted and dashed lines in (A) are guides to the eye, indicating conductance's oscillation periods. (**C**) Line trace through (B) at $V = 1.3$ mV. (Inset) Line trace through (A) at $V = 0$.

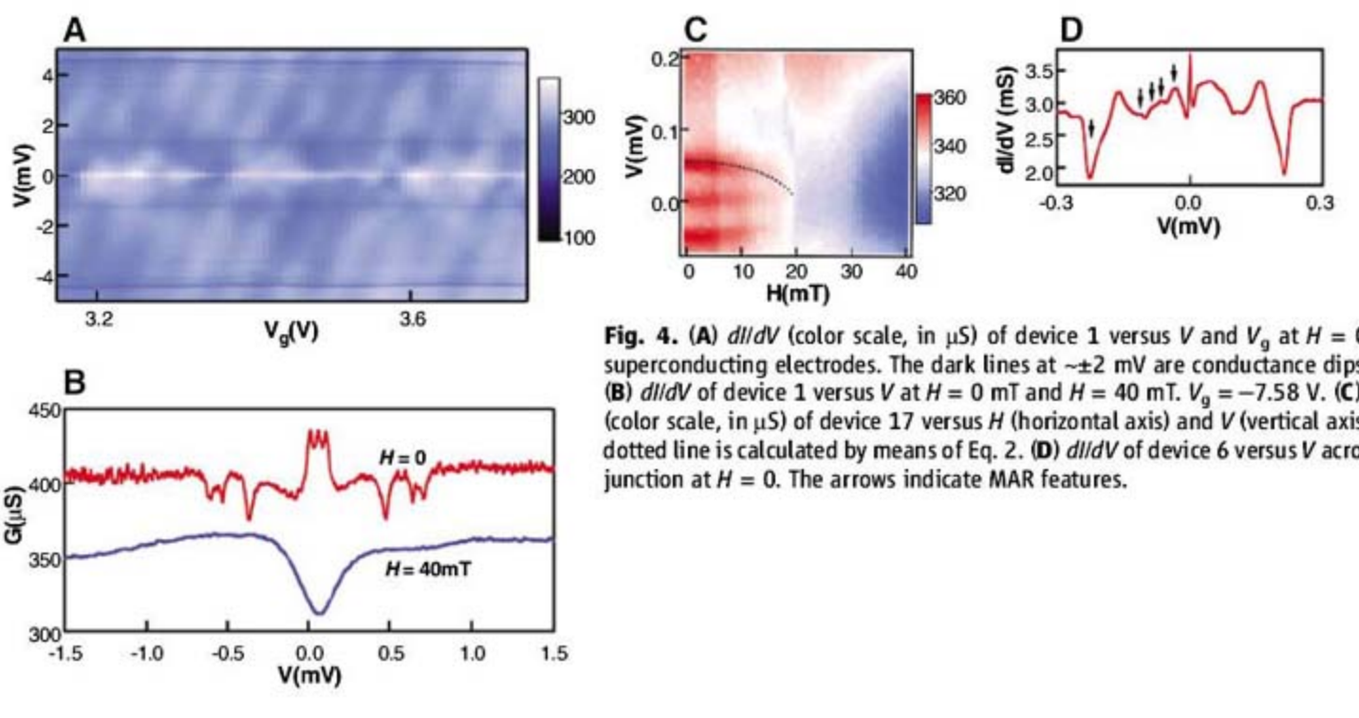

Fig. 4. (**A**) *dI/dV* (color scale, in μS) of device 1 versus V and V_g at $H = 0$ with superconducting electrodes. The dark lines at ~±2 mV are conductance dips (*13*). (**B**) *dI/dV* of device 1 versus V at $H = 0$ mT and $H = 40$ mT. $V_g = -7.58$ V. (**C**) *dI/dV* (color scale, in μS) of device 17 versus H (horizontal axis) and V (vertical axis). The dotted line is calculated by means of Eq. 2. (**D**) *dI/dV* of device 6 versus V across the junction at $H = 0$. The arrows indicate MAR features.

where σ_{min} decreases with increasing aspect ratio and reaches G_0 when $W >> L$; in contrast, devices with large source-drain separations and areas display a near-universal value of $\sigma_{min} \sim 3$ to 4 G_0, independent of device geometry, suggesting diffusive transport. The transition between the two regimes appears to take place when $L \sim 1$ μm and/or $A \sim 1$ μm^2, which may be induced by inhomogeneous doping (*22*).

Focusing on small and short graphene devices and investigating ballistic charge transport away from the charge neutrality point, we perform nonlinear transport spectroscopy by measuring the differential conductance (dI/dV) of the devices at 260 mK as functions of V_g and source-drain bias V. A small perpendicular magnetic field (~40 mT) suppresses superconductivity in the Al electrodes. The data, shown as 2D color plots, (Fig. 3, A and B), display patterns of crisscrossing lines, indicating periodic conductance oscillation with both V and V_g (Fig. 3C). Similar patterns are observed in both single-layer and bilayer devices and in both hole- and electron-doped regimes. Such periodic conductance oscillations, also observed in carbon nanotubes (*23*), arise from quantum interference of multiply reflected paths of electron (and hole) waves between two partially transmitting electrodes, whereas the charges' wavelength is tuned by bias or V_g.

In carbon nanotubes, the interference pattern is typically characterized by a single characteristic energy scale $E_0 = \frac{hv_F}{2L_0}$, where $v_F \sim 10^6$ m/s is the Fermi velocity of graphene and nanotubes and L_0 is the distance between successive reflections, given by the source-drain separation in nanotubes (*23*). In contrast, in graphene devices, we generally observe several frequencies with different energy scales. An example is shown in Fig. 3A, where a large period and a small period are outlined by dotted and dashed lines, respectively. This distinction between nanotubes and graphene devices lies in their dimensionality: One is a 1D device with well-defined electron paths, whereas the other is 2D and the electron trajectories can be quite complicated, because various electronic resonator modes (and hence energy scales) can be excited (*24*). Nevertheless, because the length $2L_0$ yields the minimum length over which electrons and holes remain phase coherent, we estimate the phase coherence length L_ϕ in graphene by identifying the smallest energy scale in each $dI/dV(V_g, V)$ plot. For our devices, $E_{0,min}$ are determined to be ~ 0.7 to 1.5 meV, corresponding to $L_\phi \sim 3$ to 5 μm at 260 mK, in agreement with values extracted from weak localization measurement (*4*).

The long phase coherence length of charges in graphene suggests a possible experimental realization of an Andreev billiard. Such a device is also a Josephson junction (*25*), expected to exhibit unusual phenomena such as specular Andreev reflections (*9*, *10*). Superconducting order is also predicted to emerge in pure and doped graphene (*26*). We repeat measurements of $dI/dV(V_g, V)$ at $H = 0$ with superconducting Al electrodes, thus realizing an Andreev billiard. As shown in Fig. 4A, the interference pattern persists, with an additional bright, horizontal band around zero bias, indicating enhanced conductance (up to 100%) that persists through both the resonance and antiresonance of the interference patterns [for high-bias conductance dips, see (*13*)].

A detailed examination of the low-bias region reveals a single peak at zero bias, and two or more additional peaks at $V \leq 2\Delta/e$, where Δ is the energy gap of Al (Fig. 4, B to D). The single conductance peak at $V = 0$ has been observed in nanotubes (*27*–*29*) and attributed either to a dissipative quasiparticles current (*27*) or to a manifestation of supercurrent (*28*). The subgap features at finite $V \leq 2\Delta/e$ results from multiple Andreev reflections (MARs) (*30*), where an electron from a normal metal incident at a superconductor is reflected as a hole, while transferring charge $2e$ by forming a Cooper pair in the superconductor. For a superconductor/normal metal/superconductor (S/N/S) junction, an electron may be reflected between the two N/S interfaces several times, gaining energy eV each time it transverses the junction, giving rise to features in dI/dV at constant voltages $V_i = \frac{2\Delta}{ie}$, where i is an integer. For the data shown in Fig. 4B, we estimate $2\Delta = 105$ μeV and $V_2 = 55$ μV. For different devices, the observed values of 2Δ range from 105 to 250 μeV, which is lower than the bulk value ~360 μeV. The reduced gap is attributed to the presence of the Pd adhesion layer.

For small H, we expect V_i to follow the classical Bardeen-Cooper-Schrieffer functional form of $\Delta(H)$

$$V_i(H) = V_i(0)\sqrt{1-\frac{H^2}{H_c^2}} \qquad (2)$$

where H_c is the critical field of Al. Figure 4C shows a plot of $dI/dV(H, V)$ for device 17, where the enhanced conductance peaks appear as the three red bands near zero bias. The positions of these peaks move to lower bias with increasing H, in excellent agreement with the dotted line, which is calculated by means of Eq. 2 and by taking $H_c = 19.5$ mT and $V_2(0) = 55$ μV directly from the data.

Up to five MAR features are observed in our devices, as shown in Fig. 4D, which plots dI/dV of device 6 as a function of voltage V across the junction. Positions of the MAR features, indicated by arrows, are 221, 110, 75, 53, and 31 μV, corresponding to $i = 1, 2, 3, 4$, and 7, respectively. Because the ith MAR feature implies electrons and holes propagate across the normal region ~i times without backscattering (*30*), our observation of several MAR features attests to the ballistic nature of transport in graphene.

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Supporting Online Material

www.sciencemag.org/cgi/content/full/317/5844/1530/DC1
Materials and Methods
SOM Text
Figs. S1 and S2
Table S1
References

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Early Archaean Microorganisms Preferred Elemental Sulfur, Not Sulfate

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Microscopic sulfides with low $^{34}S/^{32}S$ ratios in marine sulfate deposits from the 3490-million-year-old Dresser Formation, Australia, have been interpreted as evidence for the presence of early sulfate-reducing organisms on Earth. We show that these microscopic sulfides have a mass-independently fractionated sulfur isotopic anomaly ($\Delta^{33}S$) that differs from that of their host sulfate (barite). These microscopic sulfides could not have been produced by sulfate-reducing microbes, nor by abiologic processes that involve reduction of sulfate. Instead, we interpret the combined negative $\delta^{34}S$ and positive $\Delta^{33}S$ signature of these microscopic sulfides as evidence for the early existence of organisms that disproportionate elemental sulfur.

The availability and speciation of sulfur in the Archaean atmosphere-ocean system must have played an important role in the early evolution of life on Earth. The different oxidation states of this element (e.g., S^{2-}, S^{-}, S^0, $S_2O_3^{2-}$, SO_3^{2-}, SO_4^{2-}) can all act as an important source of energy for different types of sulfur-metabolizing organisms. It has been suggested that the large sulfur isotopic fractionation of sulfides (e.g., pyrite, FeS_2) in marine sediments relative to contemporaneous sulfate [e.g., gypsum ($CaSO_4$) or barite ($BaSO_4$)] provides a record of microbial sulfate reduction over time (*1*–*7*), because sulfate-reducing organisms preferentially process light over heavy sulfur isotopes (^{32}S relative to ^{34}S), leading to sulfide minerals (e.g., pyrite) with negative $\delta^{34}S = \{[(^{34}S/^{32}S)_{sample}/(^{34}S/^{32}S)_{std} - 1] \times 1000\}$ values (*8*). The resulting isotopic difference between sulfides and sulfates ($\delta^{34}S_{sulfide} - \delta^{34}S_{sulfate} = -20$ to $-30‰$) can be traced back to 2700 to 2500 million years ago (*3*, *5*). In older rocks, a much smaller isotopic difference is preserved ($\delta^{34}S_{sulfide} - \delta^{34}S_{sulfate} < -10‰$), which could indicate either that microbial sulfate reduction was absent in the Early Archaean or that microbial sulfate reduction operated under low seawater-sulfate concentration (*7*). These low sulfate concentrations would be consistent with low oxygen concentrations in the Archaean atmosphere and surface ocean (*6*, *7*). An exception to this general trend, however, is the record of strongly negative $^{34}S/^{32}S$ values of microscopic sulfides hosted in barite of the 3490-million-year-old chert-barite deposit at North Pole [Dresser Formation, Western Australia (*1*, *2*)]. It has therefore been suggested that the record of microbial sulfate reduction extends into the Early Archaean and may reflect local enrichment of sulfate in these environments (*1*).

Here we report multiple–sulfur isotope analyses (^{32}S, ^{33}S, ^{34}S) of sulfides and sulfates from drill-core samples from the chert-barite deposit at North Pole and show that metabolic pathways other than sulfate reduction can account for the microscopic sulfides with negative $^{34}S/^{32}S$ values. In the anoxic and strongly hydrothermally influenced marine environment of the Early Archaean, organisms using reduced to intermediate forms of sulfur such as S^0, $S_2O_3^{2-}$, and SO_3^{2-} were likely more common than sulfate-reducing organisms (*9*, *10*). Sulfides that form from the metabolism of S^0, $S_2O_3^{2-}$, and SO_3^{2-} may also result in significantly lower $^{34}S/^{32}S$ ratios relative to abiologic forms of sulfide (*11*). This mass-dependent isotope fractionation ($\delta^{34}S$) therefore cannot be used to distinguish such organisms from SO_4 reducers. However, in the Archaean, the different sources of sulfur used by these organisms carry distinctive mass-independent isotope ratios {anomalous $\Delta^{33}S = 1000 \times [(1 + \delta^{33}S/1000) - (1 + \delta^{34}S/1000)^{0.515}]$} (*12*–*14*). Such $\Delta^{33}S$ anomalies are produced by photochemical reactions of volcanic gases (SO_2 and H_2S) in the Archaean atmosphere and have been recognized as a tracer of the source of sulfur on early Earth (*12*–*14*). The $\delta^{34}S$ and $\Delta^{33}S$ variations for the Early Archaean record appear to be well matched by experiments of atmospheric photolysis undertaken with ultraviolet (UV) radiation of wavelength ~193 nm (*13*). In Late Archaean sediments, however, Ono *et al.* (*15*) and Kamber and Whitehouse (*16*) documented a different relation between $\delta^{34}S$ and $\Delta^{33}S$ variations and showed that their data could be bracketed by experiments undertaken with 193-nm radiation and by experiments undertaken at longer wavelengths (>220 nm) (*12*–*14*). The data for the Mesoarchaean produces another relation between $\delta^{34}S$ and $\Delta^{33}S$, adding to the complexity of the picture and raising the possibility that the interpretations of (*13*) and (*15*, *16*) may be reconciled if they reflect changes in the source reactions that occurred as the atmospheric sulfur cycle evolved from the Early Archaean to the Late Archaean. These different scenarios for atmospheric photochemical reactions suggest that S^0 and SO_4 will dominate over all other sulfur species and provide two notable sulfur sources, insoluble S^0 ($+\Delta^{33}S$) and soluble SO_4 ($-\Delta^{33}S$), that are available for sulfur metabolism. Once the $\Delta^{33}S$ anomaly is passed on to a given reservoir, it will be preserved unless there is addition of sulfur with a different $\Delta^{33}S$ composition. Figure 1 illustrates how sulfides that formed from different microbial processes would retain the $\Delta^{33}S$ anomaly of the original sulfur source.

The Dresser Formation at North Pole consists of pillowed and komatiitic metabasalt interleaved with three units of cherty metasediment. Our study focuses on the lowermost of these metasedimen-

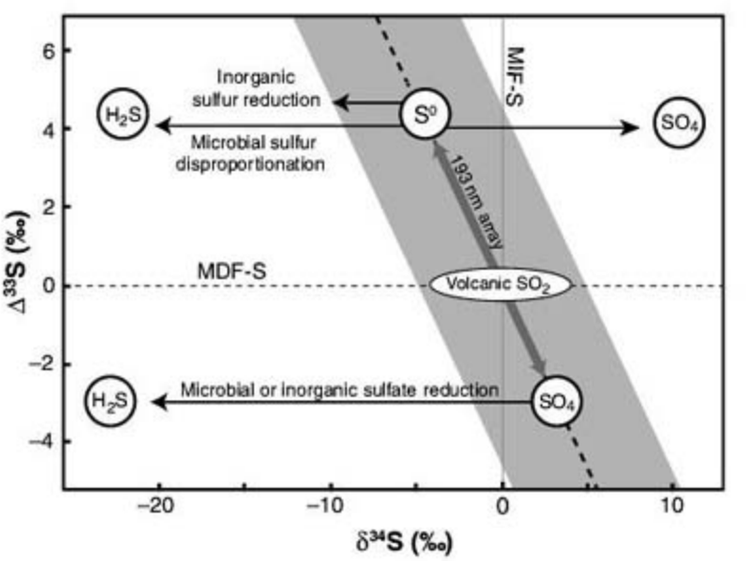

Fig. 1. Graphical representation of multiple–sulfur isotope systematics in a $\delta^{34}S$ versus $\Delta^{33}S$ plot. UV-driven photolysis of volcanic SO_2 and H_2S produces aerosols and gases (H_2S, HS, S^0, SO_2, SO_3, H_2SO_4) with both mass-independent (MIF-S, $\Delta^{33}S$) and mass-dependent isotope fractionations (MDF-S, $\delta^{34}S$) that follow experimentally determined fractionation arrays for UV radiation of 193 nm (shaded area represents a margin in $\delta^{34}S$ of ±5‰ relative to this array) (*13*). The dominant atmospheric carriers of $\Delta^{33}S$ anomalies are elemental sulfur aerosols (S^0, $+\Delta^{33}S$) and sulfuric acid aerosols (H_2SO_4) incorporated in seawater as dissolved sulfate (SO_4, $-\Delta^{33}S$). Sulfide forming from the biologic or abiologic reduction of sulfate should preserve a negative $\Delta^{33}S$ anomaly. Likewise, sulfides formed by the inorganic or microbial reduction of elemental sulfur should retain a positive $\Delta^{33}S$ anomaly, whereas microbial disproportionation of elemental sulfur should produce sulfide and sulfate that both retain a positive $\Delta^{33}S$ anomaly. Isotope fractionation associated with microbial sulfur reduction is close to zero (*26*) and therefore not shown.

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tary units known as the chert-barite unit (Fig. 2A). The age of this unit is constrained by a Pb-Pb age on galena from barite (*17*). The rocks were deposited in a shallow-water environment, possibly within a volcanic caldera (*18*, *19*), and have experienced low-grade metamorphism between 100° and 350°C (*19*). The unit consists of a succession of bedded cherts, bedded barite, volcanoclastic sandstones, and bedded carbonates. It is connected to an underlying network of barite- and silica-feeder veins. The barite veins, like the silica veins, are thought to represent conduits for hydrothermal fluid circulation (*19*–*21*). In the bedded barite, massive barite crystal fans alternate with centimeter-scale, macroscopic sulfide laminates (Fig. 2C). The barite crystals from both the bedded barite and underlying intrusive barite veins contain microscopic sulfides (Fig. 2D). The chert-barite unit has a history of complex hydrothermal alteration that is characterized by successive pulses of fluid circulation as attested by widespread silica, carbonate and sulfide overgrowth of primary textures. Several zones of relatively unaltered barite crystals, however, were found in the barite beds. We selected microscopic sulfide arrays from such unaltered barite for textural analysis [sample 88-4 of drill core Pilbara Drilling Project 2B (PDP2B)] (Fig. 2D) and sulfur-isotope and chemical analyses (samples 84-6, 89-3 of drill core PDP2B, and sample 96-6 of drill core PDP2C) (Fig. 3C and fig. S1) (*22*). Some of these microscopic sulfides in the bedded barite have up to 3.5 weight % Ni, and can contain local inclusions of pentlandite $(Fe,Ni)_9S_8$ and millerite (NiS) (fig. S1 and table S1). Specific tests with Ni-sulfide standards during the analytical procedure (*22*) show that Ni content, or the occurrence of pentlandite or millerite, has a negligible effect on sulfur-isotope analysis. Furthermore, no correlation between Ni content and $\delta^{34}S$ is present in the data set.

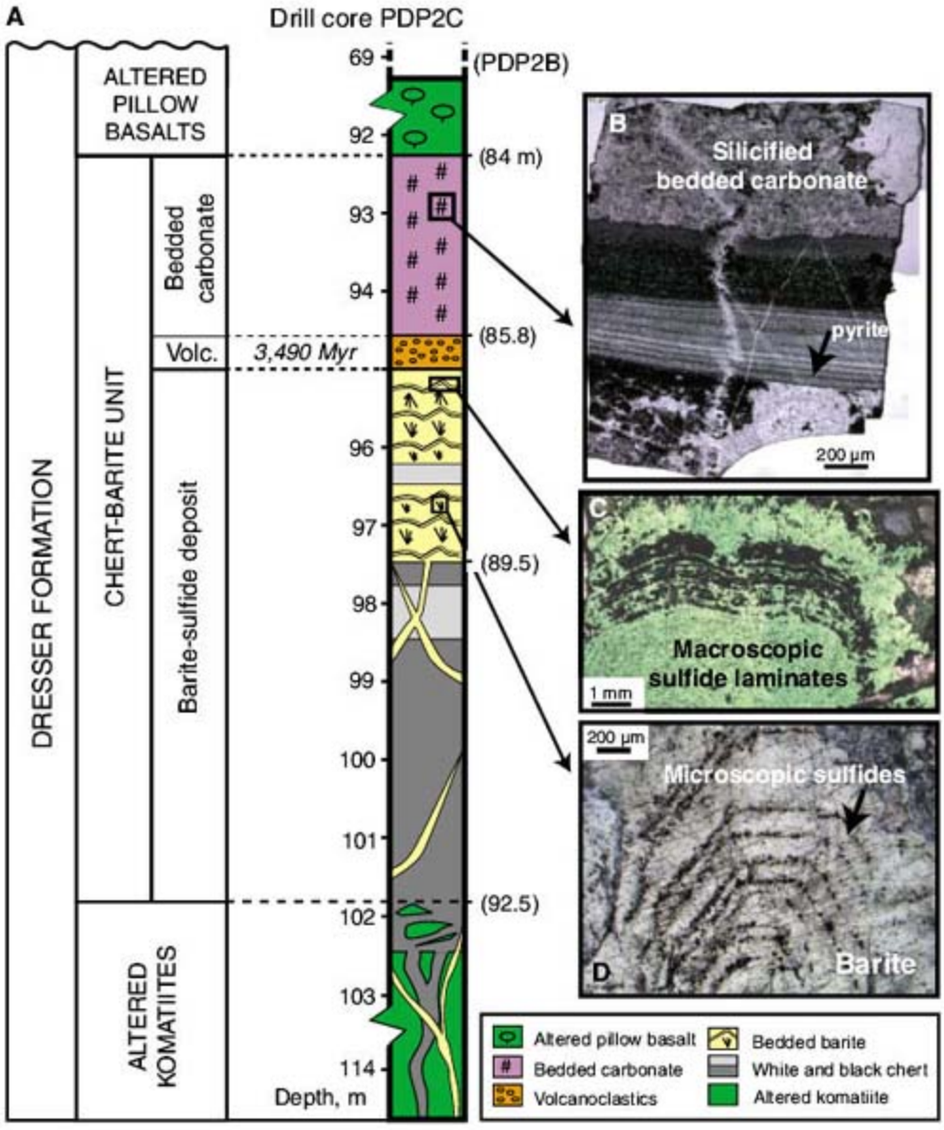

Fig. 2. (**A**) Lithological log of the Pilbara Drilling Project (*36*) for drillcore PDP2C. Five main subunits have been identified, but only three are shown for simplification. Numbers in parentheses (on the right) refer to depths (m) at which drill core PDP2B intersected the three main subunits. These include, from bottom to top, (i) hydrothermally altered komatiites intruded by silica and barite veins, (ii) barite-sulfide deposit, and (iii) volcanoclastic sandstone (Volc.) and bedded carbonate sedimentary rocks overlain by pillowed basalts. (**B** to **D**) Optical photomicrographs. (B) Silicified bedded carbonate containing thin alignments of sedimentary sulfide (sample 94.6, drill core PDP2C). (C) Macroscopic sulfide laminates (sample 95.35, drill core PDP2C). (D) Individual barite crystal containing microscopic sulfides lining barite overgrowth zones (sample 88.4, drill core PDP2B).

Our $\delta^{34}S$ data (*22*) (Fig. 3, fig. S2, and tables S2 and S3) show a limited range of values for sedimentary sulfides in the volcanoclastic sandstones and bedded carbonates (−1.4 ± 2.7‰) and macroscopic sulfide laminates in the bedded barite (−2.7 ± 1.2‰). By contrast, microscopic sulfides occurring in several barite crystals of one of the well-preserved zones within the bedded barite (fig. S1; zones 89-3a I, II, III, and zone 89.3b of drill core PDP2B) are strongly fractionated and have $\delta^{34}S$ values as low as −22.6‰. The $\delta^{34}S$ values overlap with those of previous studies, in which the mean $\delta^{34}S$ of macroscopic sulfide laminates (−0.9 ± 1.5 and −2.4‰ ± 0.8) were interpreted as unfractionated volcanogenic sulfur (*1*, *23*), and highly ^{34}S-depleted microscopic sulfides within bedded barite between −1.3 and −16.8‰ were attributed to sulfate-reducing microorganisms (*1*).

Our $\Delta^{33}S$ data (*22*) (Fig. 3, A to C, and tables S2 and S3) show distinct variations in mass-independent fractionation of sulfur isotopes (MIF-S) among the different units. Sedimentary sulfides from bedded carbonates and volcanoclastic sandstones exhibit positive $\Delta^{33}S$ anomalies of 1.0 ± 0.6‰. By contrast, the bedded barite analyzed displays a negative $\Delta^{33}S$ value of −1.2‰, which is similar to that found in (*12*) ($\Delta^{33}S = -1.0 \pm 0.1$‰ for both bedded and vein barites). Most (95%) of the microscopic sulfides in bedded barite have positive $\Delta^{33}S$ anomalies of +2.3‰ ± 1.8. Intermediate to these, the macroscopic sulfide laminates (+0.4‰ ± 0.8) show both $+\Delta^{33}S$ and $-\Delta^{33}S$ anomalies. The presence of positive and negative $\Delta^{33}S$ anomalies indicates that the source of sulfur in the chert-barite unit had cycled through the atmosphere and was introduced to the ocean to be subsequently incorporated in the seafloor sediments as insoluble elemental sulfur (S^0, represented by sulfides in bedded carbonates and volcanoclastic sandstones) or deeper into the sedimentary succession as soluble sulfate (represented by barite in the bedded and vein barite).

The observed positive $\Delta^{33}S$ of the sedimentary sulfides (Fig. 3A), macroscopic sulfide laminates (Fig. 3B), and microscopic sulfides (Fig. 3C) requires reactions involving S^0. The initial $\delta^{34}S$ of S^0 that reached the ocean floor is unknown. This value can be constrained if we assume that the SO_2-photolysis array at UV radiation of wavelength 193 nm documented for the Early Archaean (*13*) can be used to establish the array on which both initial S^0 and SO_4 must lie (Fig. 1). We used the mean $\delta^{34}S$ (+4.7‰) and $\Delta^{33}S$ (−1.0‰) values of barite (fig. S2) (*1*, *12*, *23*) as a point of reference for the precise alignment of the theoretical 193-nm array (Fig. 3, A to C) and determined that the initial S^0 must have had a $\delta^{34}S$ between −3 and +3‰. Most sulfides with positive $\Delta^{33}S$ anomalies show a limited range of $\delta^{34}S$ values, with fractionation relative to the S^0 source between 0 and −7‰. These sulfides could have formed through abiologic reduction or disproportionation of elemental sulfur to sulfide

during hydrothermal alteration, which can produce $\delta^{34}S$ isotope fractionations of only a few per mil at temperatures below 300°C [<6‰ for S^0-FeS_2 reduction (*24*), and <3‰ for S^0 disproportionation (*25*)]. Alternatively, microbial reduction of elemental sulfur to H_2S, which does not produce notable isotopic fractionation (*26*), could also explain the negligible ^{34}S depletion of these sulfides.

The microscopic sulfides within the well-preserved barite crystals (zones 84-6, 89-3b, and two microscopic sulfides of zone 89-3a in drill core PDP2B; zone 96-6 of drill core PDP2C) have $\delta^{34}S$ and $\Delta^{33}S$ values that lie on a well-defined array (broken line in Fig. 3C) parallel to the experimentally determined 193-nm MIF-S array. This finding supports the view that the 193-nm radiation was the dominant UV source during the Early Archaean (*13*).

Other microscopic sulfides (fig. S1; zones 89-3a I, II, and III and zone 89.3b of drill core PDP2B) are depleted in $\delta^{34}S$ by as much as ~23‰ relative to the S^0 source (Fig. 3C). Most of these strongly ^{34}S-depleted microscopic sulfides show positive $\Delta^{33}S$ anomalies and therefore cannot be explained by microbial sulfate reduction, as they would necessarily display negative (SO_4-derived) $\Delta^{33}S$ anomalies, not positive (S^0-derived) $\Delta^{33}S$ anomalies. Based on the same line of reasoning, certain abiologic reactions can be ruled out as well. The reduction of SO_4 in the presence of a metal catalyst during low-temperature (<350°C) hydrothermal circulation (*24*) can lead to sulfides with a strong ^{34}S depletion. Such sulfides, however, would also inherit a negative $\Delta^{33}S$, not the observed positive $\Delta^{33}S$. Another abiologic process—low- to medium-temperature (<400°C) hydrolysis of SO_2 in relatively oxidizing magmatic fluids (*27*)—can be ruled out as well because it implies a common origin of the reaction products and therefore requires that both sulfides and surrounding sulfates display the same $\Delta^{33}S$ anomaly.

Three microscopic sulfides display a negative $\Delta^{33}S$ (zone 89-3a in drill core PDP2B) (Fig. 3C). These microscopic sulfides could be the product of microbial SO_4 reduction, abiologic SO_4 reduction associated with low-temperature hydrothermal circulation, or both. A microbial origin of such microscopic sulfides therefore cannot be ruled out but is controversial, and strongly depends on the inferred depositional environment: either shallow marine evaporite (*1*) or hydrothermal deposit (*28*).

Thus, microbial processes involving S^0 best explain the large range of $\delta^{34}S$ fractionations recorded by the microscopic sulfides with positive $\Delta^{33}S$ anomalies. As shown above, these $\delta^{34}S$ fractionations are higher than the range of fractionations observed for modern sulfur-reducing microbes (*26*). Microbial disproportionation of S^0 to H_2S and SO_4^{2-} can lead to a depletion in ^{34}S by up to 16‰, and most disproportionating organisms produce fractionations smaller than 8‰ (*11*, *29*). Consortia of different types of sulfur-metabolizing organisms (S^0 disproportionators versus H_2S oxidizers), however, could have driven the $\delta^{34}S$ down during repeated cycling of this S^0 source. Such a process is described by Canfield and Thamdrup (*30*) to explain the discrepancy between the isotopic compositions of sedimentary sulfides recorded in a broad range of environments and the known magnitude of fractionations produced by natural populations of sulfur processers. A qualitative model for $\delta^{34}S$ depletion by this process is shown in Fig. 4A. Sulfate produced during S^0 disproportionation would immediately react with Ca or Ba to form gypsum or barite, respectively. This biologically derived gypsum or barite with a positive $\Delta^{33}S$ anomaly inherited from parent elemental sulfur will be instantaneously mixed with a large reservoir of evaporative gypsum or hydrothermal barite with negative $\Delta^{33}S$ anomalies. The extent to which other intermediate sulfur species, such as $S_2O_3^{2-}$ and SO_3^{2-}, would have formed during this process is not clear (Fig. 4B). Microbial reduction or disproportionation of SO_3^{2-} can cause ^{34}S depletion as low as −33‰ (*31*, *32*) and −37‰ (*10*, *11*), respectively. We conclude, based on the overall positive $\Delta^{33}S$ of these microscopic sulfides, that the ultimate source for this metabolic sulfur-cycling was atmospherically derived S^0, not atmospherically derived SO_4. After reaching the ocean floor, insoluble particulate S^0 was incorporated in synsedimentary evaporitic gypsum (*1*) and/or hydrothermally emplaced barites (*28*). Such particles provided a solid substrate to which elemental sulfur disproportionators could attach (*33*) and use H_2, CH_4, or organic compounds as an electron donor to form H_2S (*9*, *34*). This H_2S could have been oxidized back to S^0 by biologic [e.g., anoxygenic photosynthesizers (*30*)] or abiologic reactions.

The basal positions of sulfur and sulfate metabolizers in the phylogenetic tree has led to the conclusion that these organisms could be among the most ancient of our ancestors (*9*, *34*, *35*). At present, no detailed information from gene sequencing is available for the deep branching in the phylogenetic tree of sulfur-disproportionating metabolism. The combined $\delta^{34}S$ and $\Delta^{33}S$ data presented here, however, support the early origin of this group of organisms. Although only this form of sulfur metabolism can be successfully traced in this Early Archaean environment, several

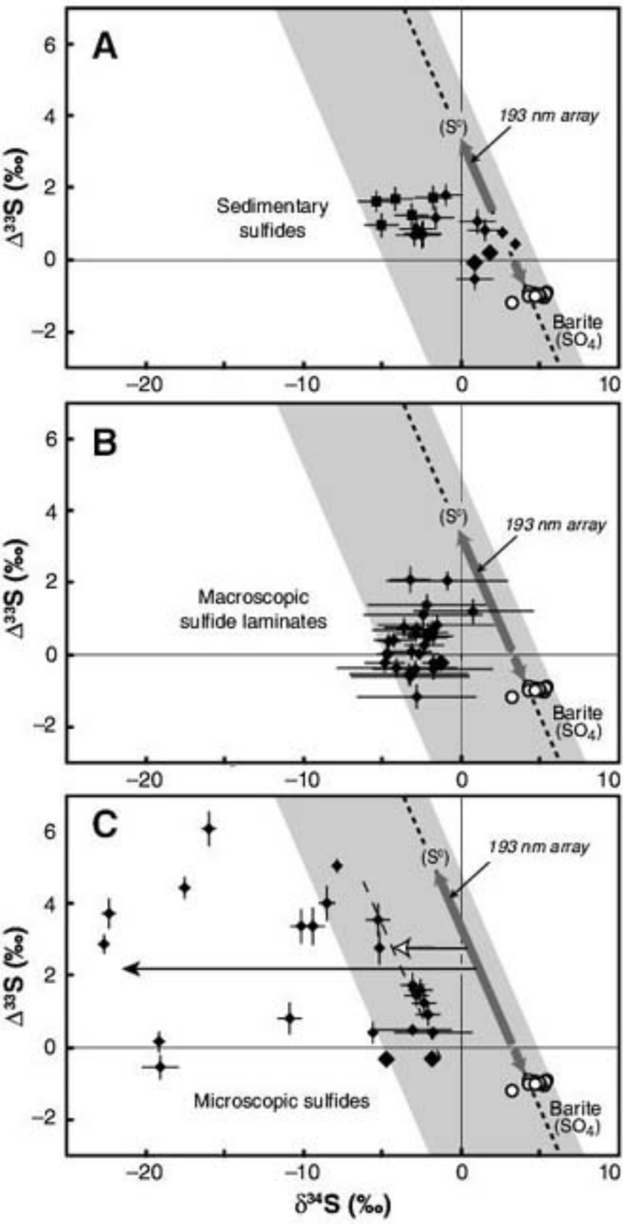

Fig. 3. Multiple–sulfur isotopic compositions of sulfides and sulfates of drillcore samples PDP2B and PDP2C. Variations of $\delta^{34}S$ with $\Delta^{33}S$ for individual sulfide analyses with the ion microprobe are shown as small symbols with 2σ error bars and for bulk barite and sulfide separates analyses as large symbols with error included in the symbol size. The 193-nm array refers to the UV-driven photolysis array at 193 nm defined in Fig. 1 (*13*) and is aligned by the mean $\delta^{34}S$ and $\Delta^{33}S$ values of North Pole barite. Bulk isotope analyses of barite [isolated white circle (this study) and cluster of white circles from (*12*)] are shown in all diagrams for comparison. (**A**) Sulfides from the sedimentary sequence [bedded carbonates (squares) and volcanoclastic sandstones (diamonds)]. (**B**) Macroscopic sulfide laminates mantling barite in bedded barite. (**C**) Microscopic sulfides in barite crystals from the bedded barite. The black arrow indicates the fractionation trend associated with microbial elemental sulfur disproportionation coupled to an inorganic or microbial oxidative metabolic pathway (see text). The white arrow points to fractionations produced by inorganic reduction or disproportionation, and/or microbial elemental sulfur reduction.

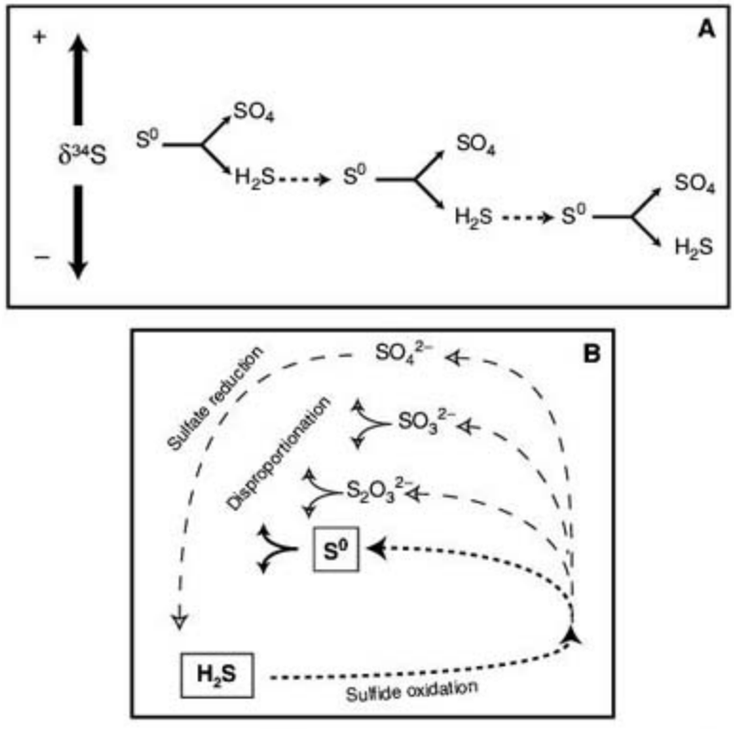

Fig. 4. Possible pathways of microbially mediated sulfur transformations and associated isotope fractionations based on (*11*) and (*30*). **(A)** Qualitative representation describing how S^0 disproportionation would lead to isotopically depleted H_2S and isotopically enriched SO_4. The H_2S that forms in this way can be reoxidized by inorganic processes or anoxygenic photosynthesizing organisms (*11*), leading to the formation of intermediate compounds such as S^0. The isotope fractionation associated with bacterial or inorganic oxidation of H_2S to S^0 is minor compared to S^0 disproportionation (*24*, *26*). Progressive disproportionation-oxidation steps will increase the ^{34}S depletion between H_2S and the initial S^0 reservoir by 20 to 30‰. **(B)** The role of other intermediate sulfur species such as $S_2O_3^{2-}$ and SO_3^{2-} in this Early Archaean environment is not clear, but it is possible that a complex consortium of sulfur-metabolizing organisms coexisted that included the cycling of these intermediate species. The three different disproportionation reactions involving S^0, $S_2O_3^{2-}$, and SO_3^{2-} are ($4S^0 + 4H_2O \rightleftharpoons 3H_2S + SO_4^{2-} + 2H^+$), ($S_2O_3^{2-} + H_2O \rightleftharpoons H_2S + SO_4^{2}$), and ($4SO_3^{2-} + 2H^+ \rightleftharpoons H_2S + 3SO_4^{2-}$) (*11*).

other forms of sulfur-based life could have been active at this time, including sulfide reducers, sulfide oxidizers, disproportionizers that used thiosulfate, or sulfite and sulfate reducers. Multiple–sulfur isotope analysis would be unable to trace the activity of elemental sulfur reducers. The preservation of a non–^{34}S-fractionated array of microscopic sulfides parallel to the 193-nm MIF-S array may be viewed as evidence for the early existence of S^0 reducers cohabitating with S^0 disproportionators.

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Supporting Online Material

www.sciencemag.org/cgi/content/full/317/5844/1534/DC1
Materials and Methods
Figs. S1 and S2
Tables S1 to S3
References

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Current-Induced Magnetization Switching with a Spin-Polarized Scanning Tunneling Microscope

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Switching the magnetization of a magnetic bit by injection of a spin-polarized current offers the possibility for the development of innovative high-density data storage technologies. We show how individual superparamagnetic iron nanoislands with typical sizes of 100 atoms can be addressed and locally switched using a magnetic scanning probe tip, thus demonstrating current-induced magnetization reversal across a vacuum barrier combined with the ultimate resolution of spin-polarized scanning tunneling microscopy. Our technique allows us to separate and quantify three fundamental contributions involved in magnetization switching (i.e., current-induced spin torque, heating the island by the tunneling current, and Oersted field effects), thereby providing an improved understanding of the switching mechanism.

The increase of hard disk and memory capacities is a result of continuously decreasing bit sizes. For example, the area of one bit in today's magnetic hard disks is on the order of $(60\,nm)^2$. Two distinct effects are used to read and write information: The giant magnetoresistive effect is used for reading, whereas writing is done by a magnetic field. When exceeding a certain limit of bit density, however, switching the magnetization of one bit may also affect the

magnetization of nearby bits because of the nonlocal character of magnetic fields, thereby accidentally destroying stored information. One solution may be the substitution of magnetic switching fields by a spin-polarized current locally exerting a magnetic torque that leads to the reversal of magnetization at sufficient current density, as has been proposed theoretically (*1*, *2*) and demonstrated experimentally based on lithographically fabricated nanopillar devices (*3*–*7*). This technique is expected to strongly reduce the circuit complexity and enable a further miniaturization of data storage devices, because the same electrical line to address a bit could be used to read information at low currents (by measuring the magnetoresistance) and write information at high currents (by the spin-torque effect).

Spin-polarized scanning tunneling microcopy (SP-STM) (*8*, *9*) is a powerful tool used to determine the magnetization state of nanostructures with spatial resolution down to the atomic scale. In addition, the same SP-STM tip that reads out the magnetization information at low tunneling currents may also serve as a highly localized source or drain of spin-polarized electrons at high tunneling currents, thereby locally exerting a magnetic torque that can reverse the magnetization of an individual monodomain nanoparticle. We report on experiments investigating the effect of high (up to 2 μA) spin currents tunneling through a vacuum barrier. Estimating a lateral resolution of 5 Å (*10*), we achieve local current densities of up to 2.5×10^8 A/cm^2. Fe nanoislands at the superparamagnetic limit are observed that, because of thermal agitation, switch their magnetization between two degenerate states (*11*, *12*). With increasing current, we observe a marked lifetime asymmetry of the two otherwise degenerate orientations, thereby demonstrating that a single scanning tunneling probe can combine reading and writing capabilities at high lateral resolution.

SP-STM also grants an ideal tunneling magnetoresistance (TMR) device with vacuum serving as an insulating barrier, thereby excluding any structural inhomogeneities or interface imperfections known from lithographically fabricated junctions. The high spatial resolution of current-induced magnetization switching (CIMS) with SP-STM also provides insight into the details of the processes involved in the magnetization reversal being inaccessible in experiments with buried interfaces. In general, the switching process can be described within a simple macrospin model. However, it was found that in some cases this model fails and has to be extended to the combined action of spin injection and the Oersted field that is induced by any flowing current (*13*). Our experiments on the spatial distribution of the lifetime asymmetry at high spin-polarized tunneling currents allow us to clearly separate and quantify spin-torque effects and influences of the Oersted field.

The SP-STM experiments were performed in an ultrahigh vacuum (UHV) system, with a preparation chamber for tip and sample treatment and an analysis chamber for sample surface characterization. A satellite of the analysis chamber contains a home-built variable-temperature scanning tunneling microscope with a current amplifier suitable for high-current applications. In both chambers, the base pressure is below 10^{-10} mbar. A W(110) substrate was cleaned by cycles of annealing [temperature (T) ≈ 1500 K] in oxygen and a subsequent high-temperature flash ($T \approx$ 2300 K) in UHV. About 0.14 atomic layers (AL) of Fe were evaporated from an e-beam–heated rod at a rate of 1.2 AL per minute at pressure $P \leq 2 \times 10^{-10}$ mbar onto the substrate held at room temperature. This leads to the formation of pseudomorphic Fe islands with a height of a single atomic layer. Topographic STM images were recorded in the constant-current mode. The differential tunneling conductance dI/dU was measured by adding a small ac modulation voltage (U_{mod} = 40 mV) to the sample bias and detecting the resulting modulation of the tunneling current by lock-in technique. We used antiferromagnetic Cr-covered W tips, which exhibit no significant stray field and are sensitive to the in-plane sample magnetization (*14*). The spin-dependent contribution to the dI/dU signal scales with cos α, where α is the angle between the magnetization directions of the tip, $\vec{m}_T$, and sample, $\vec{m}_S$ (*9*).

The topography of a 0.14-AL Fe/W(110) sample at T = 56 K (Fig. 1A) shows monolayer islands of typical diameters between 2 and 6 nm. These islands are ferromagnetic, with an in-plane easy axis along the [1$\bar{1}$0] direction (*11*, *12*), and because of their small sizes, they are monodomain particles. Whereas the Curie temperature of the extended monolayer is about 220 K (*15*), the magnetic dI/dU image (Fig. 1B) shows that the nanoislands do not exhibit a stable magnetization. A high (bright) or low (dark) dI/dU signal represents a magnetization oriented parallel or antiparallel with respect to the magnetization of

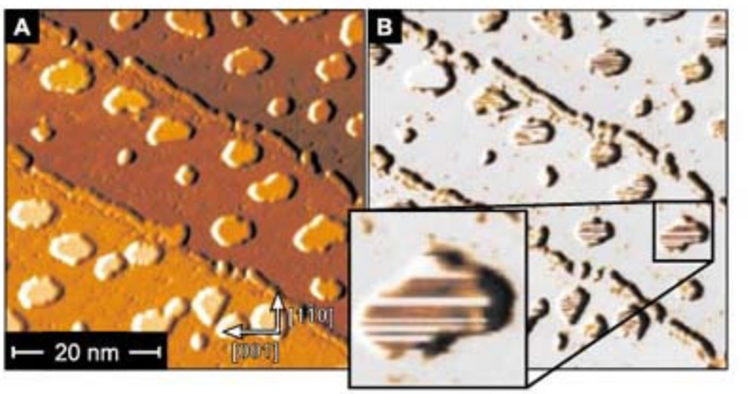

Fig. 1. (**A**) Topography and (**B**) in-plane magnetic dI/dU map of Fe monolayer islands on W(110) measured at T = 56.0 K (parameters: I = 2 nA, U = −200 mV). A dark or bright signal on the islands represents a magnetization direction parallel or antiparallel to the tip magnetization, respectively. Stripes appear on small islands (for example, in the inset) because they switch their magnetization state frequently.

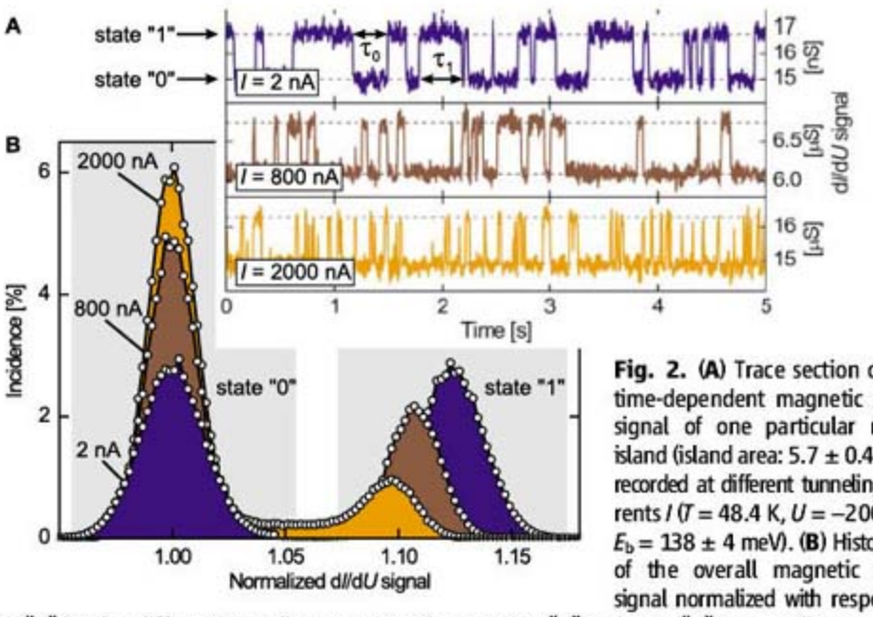

Fig. 2. (**A**) Trace section of the time-dependent magnetic dI/dU signal of one particular nanoisland (island area: 5.7 ± 0.4 nm^2) recorded at different tunneling currents I (T = 48.4 K, U = −200 mV, E_b = 138 ± 4 meV). (**B**) Histogram of the overall magnetic dI/dU signal normalized with respect to the state "0" level at different tunneling currents. Whereas state "0" and state "1" are equally populated at low currents, a substantial asymmetry toward state "0" can be recognized at high currents.

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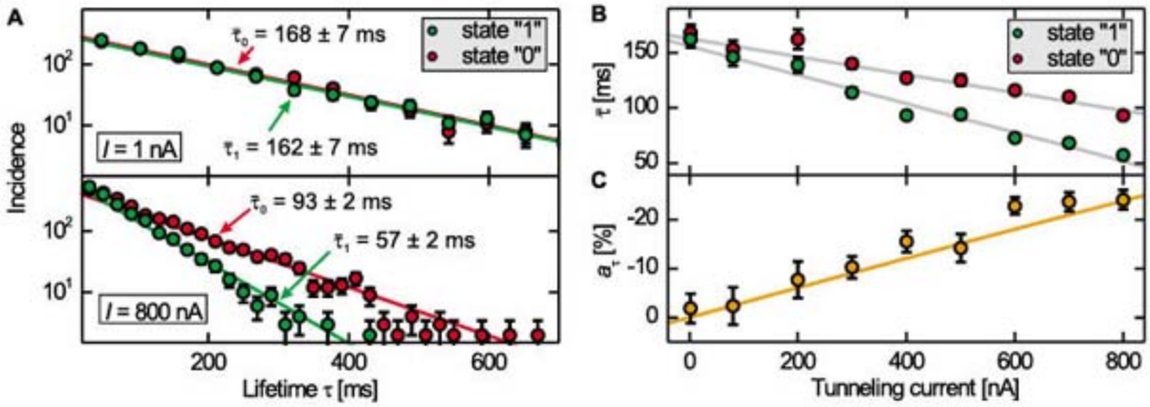

Fig. 3. **(A)** Histograms of the lifetimes τ_1 and τ_0 of states "0" and "1" measured at I = 1 nA (top panel) and I = 800 nA (bottom panel) (T = 50.6 K, U = −200 mV, E_b = 133 ± 4 meV; island area: 5.5 ± 0.4 nm^2). A decay function was fitted to the experimental data (lines) resulting in the mean lifetime $\bar{\tau}_{0,1}$. Tunneling current dependence of **(B)** the mean lifetimes $\bar{\tau}_{0,1}$ (gray lines are guides to the eye) and **(C)** the mean lifetime asymmetry a_τ. Fitting a_τ leads to a threshold current of I_c = 89 ± 4 μA. Error bars in (A) to (C) indicate SD.

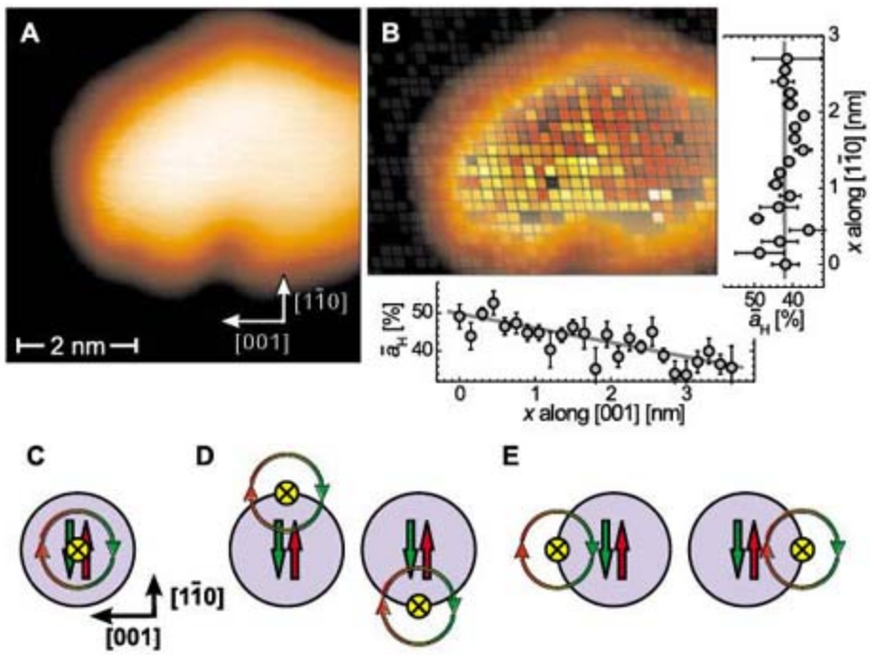

Fig. 4. **(A)** Topography and **(B)** map of the current-induced asymmetry a_H as measured with a Cr-coated probe tip at I = 600 nA and U = +200 mV (island area: 6.7 ± 0.6 nm^2; T = 55.0 K). The plots show a_H averaged in rows and columns: that is, along the [1$\bar{1}$0] and [001] directions, respectively. Although $\bar{a}_H$ is constant within the error bar (SEM) along the [1$\bar{1}$0] direction, it clearly reduces by about 16% from the left to the right side of the island (gray lines are guides to the eye). The schematic illustrates the influence of the Oersted field with the tip positioned in the center **(C)**, at the magnetic poles **(D)**, or at the charge-free side **(E)** of the nanoisland.

the atom at the tip apex. While mapping, the spin-resolved dI/dU signal on the islands frequently switches. As we know from earlier investigations on similar sample systems (*16*, *17*), such observations are characteristic for superparamagnetic switching, where the magnetization spontaneously reverses because of thermal activation.

We have recorded the magnetic dI/dU signal as a function of time, with the tip positioned stationary above the central region of small Fe nanoislands with a typical surface area of 7 nm^2 (i.e., consisting of about 100 atoms). All measurements have been performed in the constant-current mode, obtaining different tunneling currents by adjusting the tip-sample distance. For example, the traces in the panels of Fig. 2A show 5 s of the spin-resolved dI/dU signal measured on one particular island at tunneling currents of I = 2, 800, and 2000 nA. Figure 2B shows the histograms of the magnetic dI/dU signal recorded over a much longer period (700 s) normalized with respect to the lower level at the different tunneling currents. At a low tunneling current, the dI/dU signal statistically switches between two discrete levels: states "0" and "1" (top panel of Fig. 2A). The respective histogram of Fig. 2B reveals that both states occur with the same probability. This finding is as expected because the two magnetization states are energetically degenerate and therefore should be populated equally. As I is increased, however, an imbalance between states "0" and "1" builds up until one state clearly dominates, as shown for I = 2000 nA. Furthermore, with increasing tunneling current, a tendency of decreasing dI/dU signal contrast is observed. This decrease might be caused by a distance-dependent polarization of the electronic states involved in the tunneling process. Hence, spin-polarized tunneling currents lead to a splitting of the two (otherwise degenerate) effective activation barriers separating the two magnetization states. To quantify this imbalance, we fitted each of the histogram peaks by a Gaussian with the area $A_{0,1}$. By defining the histogram asymmetry $a_H \equiv (A_1 - A_0)/(A_1 + A_0)$, we observe asymmetries a_H = −0.7 ± 0.5%, −39.4 ± 0.7%, and −74 ± 1% for I = 2, 800, and 2000 nA. In agreement with experiments on planar junctions, an opposite spin-polarization was observed for tunneling currents flowing in the opposite direction (*18*).

The microscopic processes causing the asymmetries can be understood by a statistical analysis of the lifetimes of states "0" and "1," τ_0 and τ_1, as defined in the top panel of Fig. 2A. Figure 3A shows lifetime histograms of τ_0 and τ_1 of one particular Fe nanoisland measured at I = 1 nA (top panel) and I = 800 nA (bottom panel) with the same tip. Fitting with a decay law results in the respective mean lifetimes $\bar{\tau}_0$ and $\bar{\tau}_1$. At low tunneling current, $\bar{\tau}_0$ and $\bar{\tau}_1$ are very similar. A different behavior is observed at high tunneling currents, where the mean lifetime is found to depend strongly on the relative magnetization direction between the tip and sample. In this case, for I = 800 nA, one state has a much higher mean lifetime than the other. Plotting $\bar{\tau}_0$ and $\bar{\tau}_1$ as a function of the current reveals a trend from equal lifetimes at low current to an imbalance at high current. Furthermore, the mean lifetime of both states decreases with increasing current, an effect that we attribute to Joule heating due to the high tunneling current. Assuming that the energy of the tunneling electrons is dissipated within about 1 to 2 nm, which is in rough agreement with known values of the inelastic mean free path of electrons (*19*), a simple model (*20*) indicates a temperature rise of 0.3 to 0.6 K. Our SP-STM experiments on the temperature-dependent magnetic properties of Fe nanoislands on W(110) show a consistent behavior (i.e., a switching rate that roughly doubles every 0.5 K). By defining the lifetime asymmetry $a_\tau \equiv (\bar{\tau}_1 - \bar{\tau}_0)/(\bar{\tau}_1 + \bar{\tau}_0)$, we obtain values of up to –25% for I = 800 nA

(Fig. 3C). The degeneracy of the effective activation barriers is lifted at high tunneling currents, and based on the Arrhenius-like switching behavior, the mean lifetimes $\bar{\tau}_{0,1}$ can be expressed as (*21*, *22*)

$$\bar{\tau}_{0,1} = \upsilon_a^{-1} \exp\left[\frac{E_b}{k_B T}\left(1 - \frac{I}{I_c}\right)\right] \quad (1)$$

where υ_a is the attempt frequency, E_b is the effective activation barrier of the island at zero current, k_B is the Boltzmann constant, I denotes the tunneling current, and I_c is the threshold current to switch the magnetization at $T = 0$ K. E_b was determined by a variation of T from 50.6 to 48.5 K and derivation of the respective mean lifetimes $\bar{\tau}_{0,1}$ at low tunneling currents ($I = 1$ nA). For the particular island of Fig. 3, we find $E_b = 133 \pm 4$ meV, leading to a threshold current of $I_c = 89 \pm 4$ μA. Because such high currents are not realizable within the tunneling regime, we do not expect to switch islands of the given dimensions at $T \approx 0$ K. Assuming an effective tunneling area given by the lateral STM resolution, the corresponding threshold current density is $(113 \pm 5) \times 10^8$ A/cm^2. This value is, by two to three orders of magnitude, higher than the current density used in similar experiments based on TMR devices (*23*), which may be attributed to the fact that, in contrast to planar junctions, the current density is not distributed homogenously on the whole nanoisland but acts very locally. The splitting of the effective activation barrier ΔE due to spin-torque effects can be quantified by

$$\Delta E = k_B T \ln \frac{1 + a_\tau}{1 - a_\tau} \quad (2)$$

where a_τ is the lifetime asymmetry. For $I = 800$ nA, the current-induced spin torque leads to an effective activation barrier splitting of $\Delta E = 1.3 \pm 0.1$ meV, which is only $\approx 1\%$ of E_b.

Using a SP-STM tip as the source or drain for spin-polarized electrons, we were able to perform spatially resolved measurements where the tip is moved to different sites of one particular nanoisland, allowing information of site-specific properties to be gained that cannot be obtained in spatially averaging experiments performed with nanopillars. Figure 4A shows the topography of a nanoisland consisting of about 100 atoms. While scanning this island with $I = 600$ nA, we measured the magnetic dI/dU signal on each of the pixels for a duration of 12 s to calculate the site-specific histogram asymmetry a_H on the basis of the corresponding datapoint histograms. The result is shown in a color-coded representation in Fig. 4B. In spite of the rather large statistical error, a gradient along the [001] direction can clearly be recognized. The effect can even be analyzed quantitatively by averaging a_H column- and row-wise: that is, along the $[1\bar{1}0]$ and the [001] directions, respectively. Whereas $\bar{a}_H$ is constant within the error at about 42% when moving the tip along the $[1\bar{1}0]$ direction, it clearly reduces by about 16% from the left to the right side of the island. The lateral tip position obviously may influence the switching behavior of the nanoisland at high tunneling currents, as illustrated in Fig. 4, C to E. If the tip is positioned above the island center, the influence of the Oersted field along the $[1\bar{1}0]$ direction, which is the easy axis of the nanoisland, cancels (Fig. 4C). In this case, pure spin-current–induced switching occurs. Likewise, no influence by the Oersted field is expected if the tip is moved from the center to either island edge along the $[1\bar{1}0]$ direction (Fig. 4D) as the effective field acting on the island is oriented perpendicular to the easy axis. Only if the tip is moved from the center along the [001] direction one magnetic state is favored over the other by the Oersted field (Fig. 4E). In this case, Oersted field effects influence the magnetic switching behavior, dependent on the tip position. A detailed analysis of the data yields that the effective activation barrier splitting of $\Delta E = -2.4 \pm 0.2$ meV at the center of the island is increased or decreased by up to 0.7 ± 0.2 meV when moving along the [001] direction to either island edge. This finding indicates that the magnetization switching is dominated by the spin torque induced by the spin-polarized current, whereas the influence of the Oersted field remains small. A simple estimation of the energy splitting caused by the Oersted field, as obtained by integrating the expected field distribution of an infinitely expanded current line over the island area, yields a Zeeman energy of up to $\Delta E_{Oersted} = \sum \vec{m} \cdot \vec{B}(\vec{r_i}) \approx 0.2$ meV [$|\vec{m}| = 2.79\mu_B$ (*24*)][i], where $\vec{m}$ is the magnetic moment, $\vec{B}$ is the Oersted field, $\vec{r_i}$ is the position of atom i, and μ_B is the Bohr magneton. This estimated value is somewhat lower than the experimental result. We attribute the difference to the oversimplified geometry of our model.

Our SP-STM studies provide insight into the details of current-induced magnetization switching that has been inaccessible in experiments with lithographically fabricated tunnel junctions. The ultimate lateral resolution of SP-STM combined with CIMS promises innovative perspectives for future data storage technologies.

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Global Pattern Formation and Ethnic/Cultural Violence

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We identify a process of global pattern formation that causes regions to differentiate by culture. Violence arises at boundaries between regions that are not sufficiently well defined. We model cultural differentiation as a separation of groups whose members prefer similar neighbors, with a characteristic group size at which violence occurs. Application of this model to the area of the former Yugoslavia and to India accurately predicts the locations of reported conflict. This model also points to imposed mixing or boundary clarification as mechanisms for promoting peace.

Over the past 100 years, more than 100 million people have died in violent conflicts (*1*). Of these deaths, a great number are attributable to ongoing local conflict between culturally or ethnically distinct groups. A scientific understanding of the underlying causes of ethnic violence could lead to policy changes that may help stop or prevent it. The existing literature (*2*–*13*) [see also bibliography of ethnic and cultural conflict in the supporting online materials (*14*)] generally considers (i) the process by which ethno-religious identity is established and if inter-

ventions could diminish its importance relative to more inclusive identities, and (ii) control mechanisms of the state and of organizations of ethnic groups and if interventions could strengthen the state while subsuming or accommodating ethnic groups within state authority. More specific social and economic factors identified in the literature as contributing to violence include oppression of minorities, economic grievances, historical precedents, competition for resources, favoritism, availability of resources for violence, security fears, mobilization by elites, weak social ties, national ethnic diversity, territorial claims, religious or political polarization, incendiary media, and international influences. Although most of these studies consider national conditions, a few consider local violence to identify the role of local socioeconomic or geographic factors (*7*–*9*). Here, we focus on an aspect of spatial population structure that has been neglected so far; we analyze the global pattern of violence and propose that many instances are consistent with the natural dynamics of type separation (*15*–*18*), a form of pattern formation (*19*) also seen in physical or chemical phase separation. Violence arises due to the structure of boundaries between groups rather than as a result of inherent conflicts between the groups themselves. In this approach, diverse social and economic causal factors trigger violence when the spatial population structure creates a propensity to conflict, so that spatial heterogeneity itself is predictive of local violence. The local ethnic patch size serves as an "order parameter," a measure of the degree of order of collective behavior, to which other aspects of behavior are coupled. The importance of collective behavior implies that ethnic violence can be studied in the universal context of collective dynamics, where models can identify how individual and collective behavior are related.

A simple model of type separation is shown in Fig. 1, A to E. The dynamics of this model assume that individuals preferentially move to areas where more individuals of the same type reside (*14*). The resulting dynamics lead to progressively larger patches ("islands" or "peninsulas") of each type. The average size of patches at a particular time can be obtained by a number of different methods. We used overlapping spatial waves that represent the spatial variation of the population density. Each wave makes a contribution proportional to its correlation with the population density (the structure factor or Fourier transform). The wavelength of the wave that has the maximum amplitude gives the average size of the patches. Other methods of obtaining the size of patches give similar results. The size of the patches grows as a characteristic power of time (Fig. 1F, inset). This behavior has been proven (*20*) to be a "universal behavior" that does not depend on many of the details of the model and therefore may be relied on to describe a large variety of systems of interacting elements; in particular, similar models have been used to describe the relation of chemical interaction energies and chemical precipitation or phase separation (*21*, *22*). The universal properties of the patterns upon rescaling of length and time also imply that a number of individual agents of the model can be aggregated into a single agent if time is rescaled correspondingly without changing the behavior at the larger scales (Fig. 1F). Thus, it is possible to consider a model agent to represent a local population, and it is not necessary to model the behavior of each individual—an impractical undertaking.

To model violence, we assume that highly mixed regions do not engage in violence, and neither do well-segregated groups, an intuitive hypothesis with empirical support (*7*). The analy-

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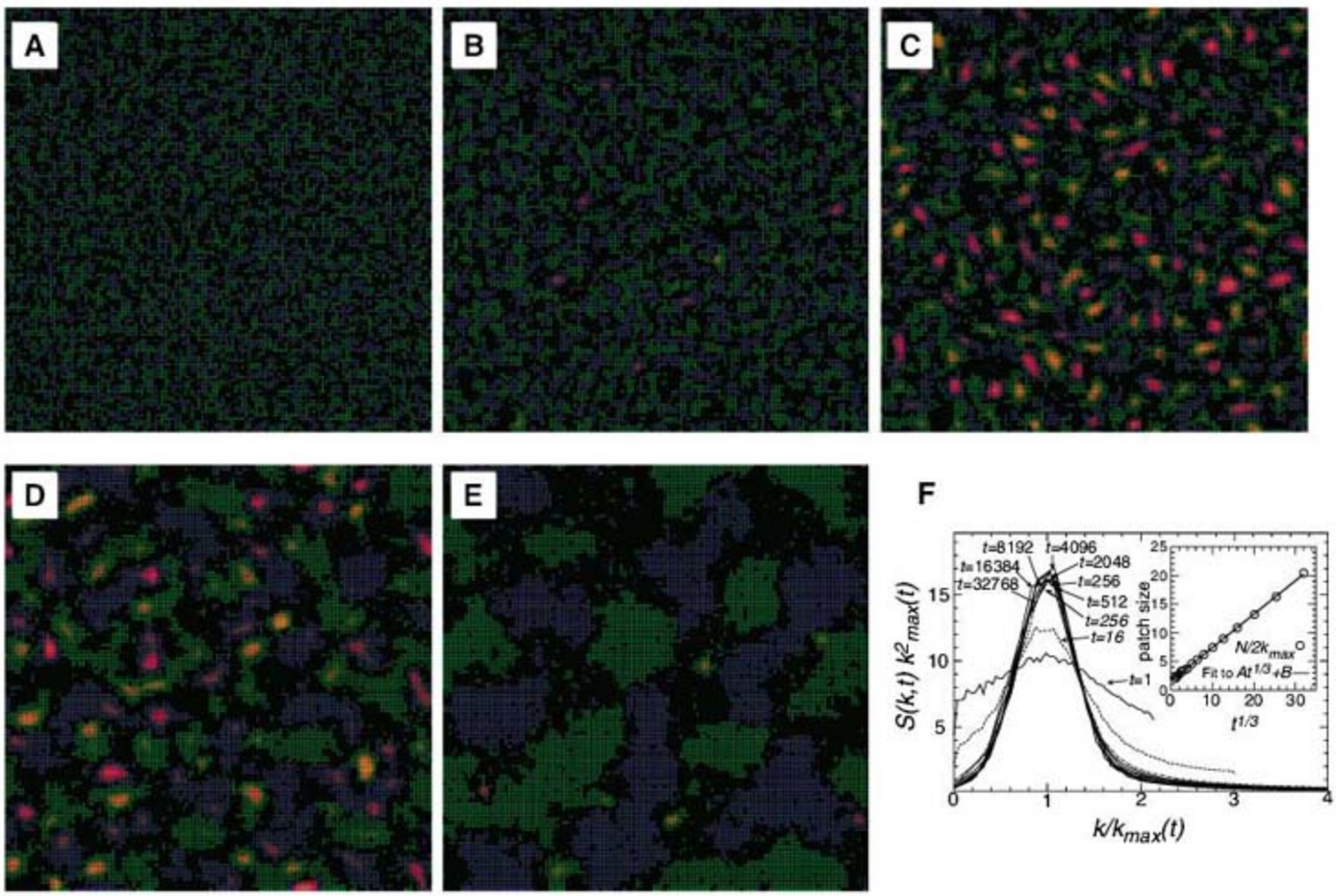

Fig. 1. Simulation of type separation with two types of agents [**(A)** to **(E)** show the system at 8, 64, 512, 4096, and 32768 attempted moves per particle, respectively]. The shape of domains (as characterized by the rescaled structure factor amplitude squared) remains constant after an initial transient (**F**), and the average size of clusters grows as a power law [inset of (F)] (*14*). Patches of a certain size that are surrounded by the other type are highlighted by red shading overlay in (A) to (E). We identify such regions with a high likelihood of conflict.

sis is applicable to communal violence and not to criminal activity or interstate warfare. In highly mixed regions, groups of the same type are not large enough to develop strong collective identities, or to identify public spaces as associated with one or another cultural group. They are neither imposed upon nor impose upon other groups, and are not perceived as a threat to the cultural values or social/political self-determination of other groups. Partial separation with poorly defined boundaries fosters conflict. Violence arises when groups are of a size that they are able to impose cultural norms on public spaces, but where there are still intermittent violations of these rules due to the overlap of cultural domains. When groups are larger than the critical size, they typically form self-sufficient entities that enjoy local sovereignty. Hence, we expect violence to arise when groups of a certain characteristic size are formed, and not when groups are much smaller or larger than this size. The model of violence depends on the distribution of the population and not on the specific mechanism by which the population achieves this structure, which may include internally or externally directed migrations. By focusing on the geographic distribution of the population, the model seeks a predictor of conflict that can be easily determined by census. This may work well because geography is an important aspect of the dimensions of social space, the dynamic coarsening process is universal, and other aspects of social behavior (e.g., isolationism, conformity, as well as violence) are correlated to it.

The predictor that we identify based on spatial census data need not describe the immediate social or institutional triggers of violence, only the conditions under which violence becomes likely. Previous research aiming to characterize ethnic conflict by census data has focused on measures of ethnic or religious "fragmentation" (*23*–*27*). Such measures characterize the diversity of a country without reference to its spatial structure, i.e., the overall proportions of ethnically distinct groups in a country. They are therefore distinct from the spatial characterization of our study. The literature is divided about whether or which correlations exist with measures of national ethnic composition. We

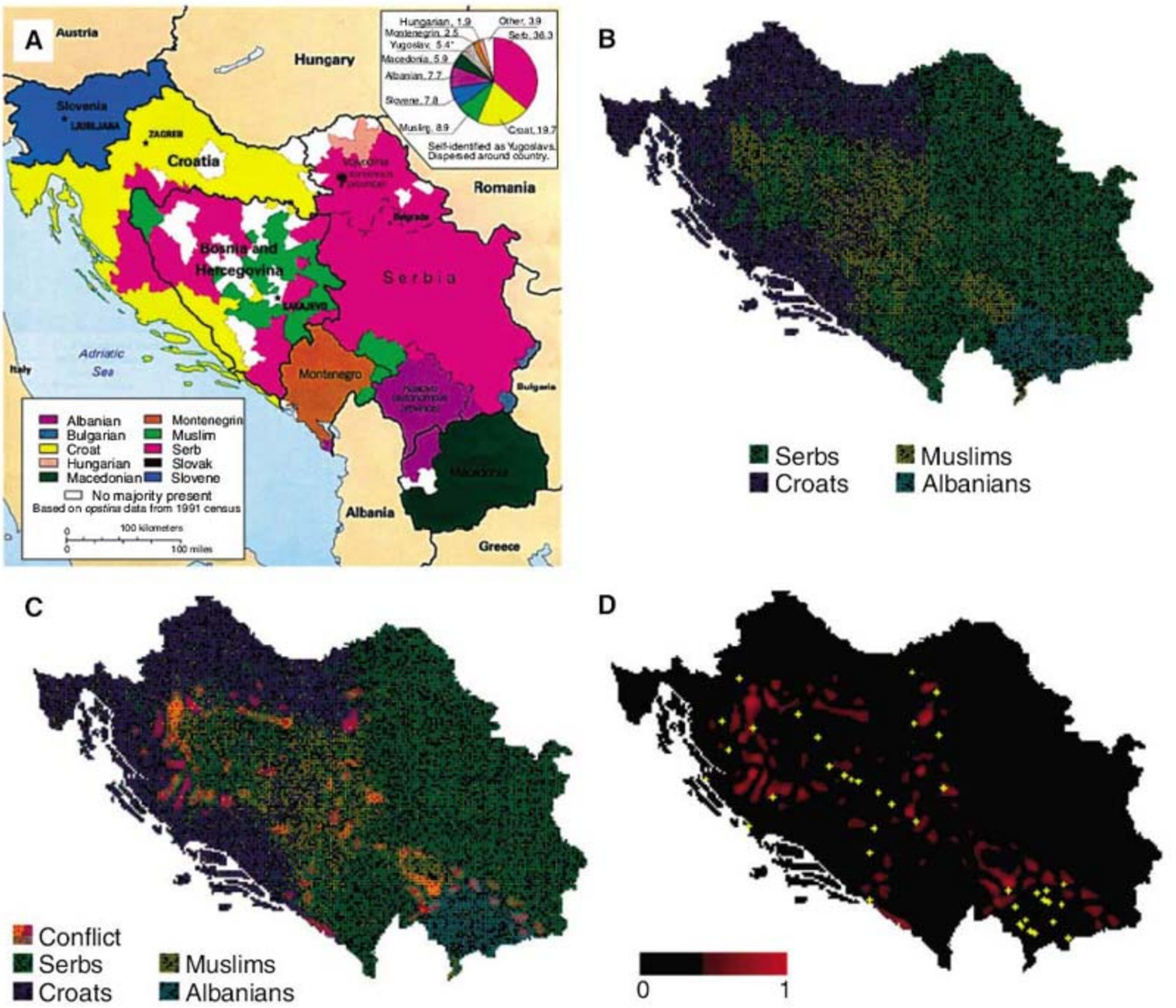

Fig. 2. (**A**) Census data from 1991 shown here in map form were converted into a spatial representation and used in an agent-based simulation shown in (**B**). Our prediction of populations likely to be in conflict with neighboring groups [red overlay, (**C**) and (**D**)] agrees well with the location of cities reported as sites of major fights and massacres [yellow dots, (D)].

find, however, that the spatial distribution of ethnic groups is a strong predictor of locations of violence.

Mathematically, the expected violence was determined by detecting patches consisting of islands or peninsulas of one type surrounded by populations of other types. We detected these features by correlation of the population for each population type with a template that has a positive center and a negative surround. To illustrate the effect of this correlation, for a particular template size, the maximum correlation over population types is superimposed as a red overlay in Fig. 1, A to E. Over time in this simulation, the patch size starts smaller, then passes through and becomes larger than the template size chosen. The specific template that we used is based on a wavelet filter (*14*, *28*–*30*). Wavelets are designed to obtain a local measure of the degree to which a certain scale of variation (wavelength) is present. Outcomes are highly robust, and other templates give similar results. Given the universality of the dynamic behavior, the diameter of the positive region of the wavelet, i.e., the size of the local population patches that are likely to experience violence, is the only essential parameter of the model. The parameter is to be determined by agreement of the model with reports of violence, though as we will see, the agreement is robust to variation of the parameter. The quality of the agreement provides a measure of the validity of the model.

To test the predictive ability of the model, we performed simulations based on census data for the former Yugoslavia and India. We assigned areas of pixelated geographic maps pixel by pixel to ethnic groups at random, but in proportion to their relative population census in the region. Although this does not reflect the physical geography or local mixing of groups in buildings and villages, over an area of multiple pixels it captures the regional composition of the census. The pixelated map serves as the beginning state for the agent model. For Yugoslavia, census data from the early 1990s before the outbreak of conflict (*31*, *32*), as shown in Fig. 2A, were captured into an agent simulation (Fig. 2B), which was used to obtain the regions of expected violence shown in Fig. 2C.

We then obtained from books (*2*), newspapers, and Internet sources (see supporting online text) the locations of reported violence for the area of the former Yugoslavia. Multiple independent sources were used to provide validation for each location of violence (*14*). We consider these reports as indicators of areas of actual violence, keeping in mind possible bias and incompleteness and that areas of widespread violence are identified only by local urban centers. In comparing such reports with model predictions, we note that the model identifies locations of groups of a particular size, but the location of the actual violence should occur somewhere in the area between adjacent groups. Despite these caveats, overlaying the locations of reported and predicted violence in Fig. 2D demonstrates a significant ability of our simple model to identify regions of reported violence. We performed statistical analyses comparing the predicted to the reported violence, evaluating the ability of the model to determine both where violence occurs and where violence does not occur. For comparison, we randomized the locations of reported violence. We defined "conflict proximity" as the distance between a given position and the nearest location of violence (predicted, reported, or randomized). We calculated Pearson's correlation and other statistical measures between the proximities of predicted and reported violence, and compared them with the same measures in relation to randomized reports. We found that the model has a correlation of 0.9 with reports (0.89 to two significant digits), a level of agreement not reached in any of 100,000 randomized trials. Moreover, the predicted results are highly robust to parameter variation, with essentially equivalent agreement obtained for filter diameters ranging from 18 to 60 km, a range that is in agreement with intuition about the size of conflict areas. Below or above this range, poorer agreement occurs. Details are provided in the supporting online text.

We studied conflict in India as a second case study of the ethnic violence model. We constructed a spatial representation of India on a district level from maps at www.censusindia.net and obtained the distribution of ethno-cultural groups from the 2001 Census data at www.indiastat.com. The result can be seen in the form of three-color maps in Fig. 3, A and B, representing the relative densities of Hindus, Muslims, Christians, Sikhs, Buddhists, and Others (primarily Jains). The agent model is shown in Fig. 3C and the prediction of ethnic violence is indicated in Fig. 3D. Predictions correspond very well to the primary locations of "extremist" violence of government reports as given by indiastat.com (Fig. 3E) and confirmed by independent sources (*14*), particularly in Kashmir, Punjab, and the states of Northeast India. Some additional areas of lesser violence were also predicted by the model, particularly Jharkhand—an eastern state created in 2000 that has recently experienced some violence (*14*, *33*). Consistent with predicted results, the violence in this region is not as prevalent as in other violence-prone areas of India. Statistical correlation measures of conflict proximity yield a correlation of 0.998 when the threshold is set above the value of predicted violence in Jharkhand. If the threshold is set lower, so that violence in Jharkhand is included in predicted but not in reported cases, the correlation falls to 0.92. Including reported violence in Jharkhand when comparing at the lower threshold increases the correlation to 0.98. Additional details are provided in the supporting online text. The range of filter diameter values for which good agreement was obtained overlaps that of the former Yugoslavia. However, it is shifted to larger values, up to ~100 km. This may reflect not only the larger granularity of data, but perhaps also the effect of violence itself on separation. Unlike Yugoslavia, in India the census was performed during ongoing violence. Because violence accelerates the process of separation, groups in conflict are likely to have separated substantially and reflect the high end of group sizes susceptible to violence.

Governmental and nongovernmental organizations are devoting increasing attention to the prevention of major conflict (*34*). Under some circumstances, social and institutional factors that affect violence might serve to suppress the triggering of violence without changing the spatial structure of the population. However, influencing the spatial structure might address the conditions that promote violence described here. Such ap-

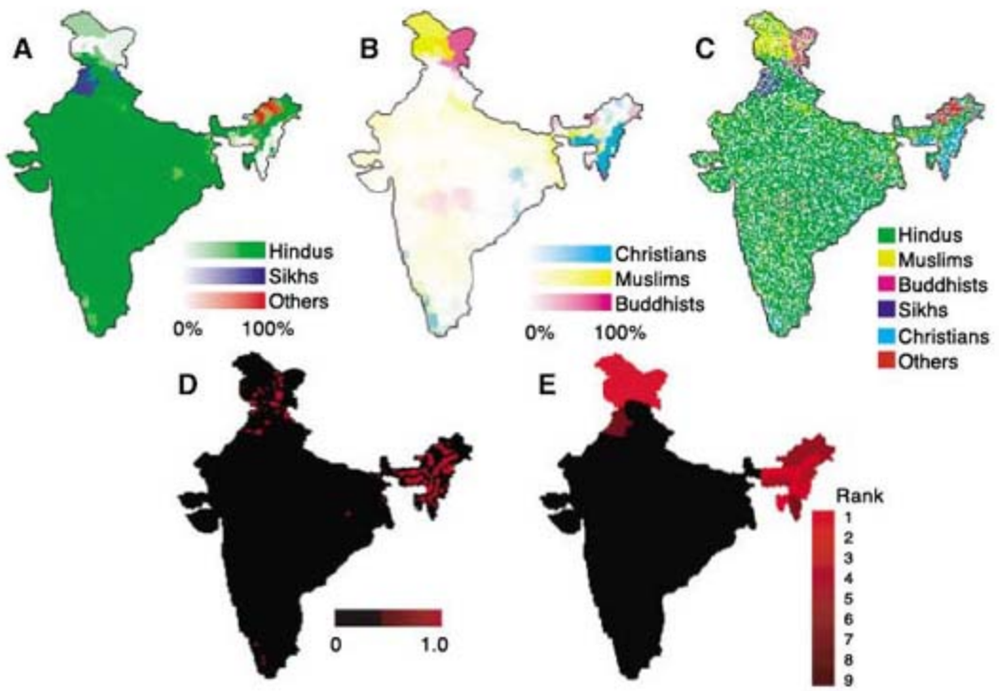

Fig. 3. (**A** and **B**) Spatial representation of Indian census data from 2001 of six indicated groups was converted into an agent-based simulation shown in (**C**). Our prediction of conflict-prone areas [red areas in (**D**)] agrees with states where major ethnic violence has been reported [red areas in (**E**)] between 1999 and 2002, with the red shading intensity corresponding to the rank order of states by number of incidents.

proaches have been and are being considered. For example, in Singapore, where 84% of the population lives in public housing (*35*), regulations that explicitly recognize the role of spatial segregation in sectarianism specify the percentage of ethnic groups to occupy housing blocks (*36*). This legally compels ethnic mixing at a scale finer than that which our study finds likely to lead to violence. Given the natural tendency toward social separation, maintaining such mixing requires a level of authoritarianism that might not be entertained in other locations. Still, despite social tensions (*37*), the current absence of violence provides some support to our analysis. The alternative approach—aiding in the separation process by establishing clear boundaries between cultural groups to prevent violence—has also gained recent attention (*38*, *39*). Although further studies are needed, there exist assessments (*39*) of the impact of historical partitions in Ireland, Cyprus, the Indian subcontinent, and the Middle East that may be consistent with the understanding of type separation and a critical scale of mixing or separation presented here.

The insight provided by this study may help inform policy debates by guiding our understanding of the consequences of policy alternatives. The purpose of this paper does not include promoting specific policy options. Although our work reinforces suggestions to consider separation, we are not diminishing the relevance of concerns about the desirability of separation or its process. Even where separation may be indicated as a way of preventing violence, caution is warranted to ensure that the goal of preventing violence does not become a justification for violence. Moreover, even a peaceful process of separation is likely to be objectionable. There may be ways to positively motivate separation using incentives, as well as to mitigate negative aspects of separation that often include displacement of populations and mobility barriers.

Our results for the range of filter diameters that provide good statistical agreement between reported and predicted violence in the former Yugoslavia and India suggest that regions of width less than 10 km or greater than 100 km may provide sufficient mixing or isolation to reduce the chance of violence. These bounds may be affected by a variety of secondary factors including social and economic conditions; the simulation resolution may limit the accuracy of the lower limit; and boundaries such as rivers, other physical barriers, or political divisions will surely play a role. Still, this may provide initial guidance for strategic planning. Identifying the nature of boundaries to be established and the means for ensuring their stability, however, must reflect local issues.

Our approach does not consider the relative merits of cultures, individual acts, or immediate causes of violence, but rather the conditions that may promote violence. It is worth considering whether, in places where cultural differentiation is taking place, conflict might be prevented or minimized by political acts that create appropriate boundaries suited to the current geocultural regions rather than the existing historically based state boundaries. Such boundaries need not inhibit trade and commerce and need not mark the boundaries of states, but should allow each cultural group to adopt independent behaviors in separate domains. Peaceful coexistence need not require complete integration.

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Supporting Online Material

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Methods
Figs. S1.1 to S4.3
SOM Text
Table S1
References
Bibliography

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Crystal Structure of an Ancient Protein: Evolution by Conformational Epistasis

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The structural mechanisms by which proteins have evolved new functions are known only indirectly. We report x-ray crystal structures of a resurrected ancestral protein—the ~450 million-year-old precursor of vertebrate glucocorticoid (GR) and mineralocorticoid (MR) receptors. Using structural, phylogenetic, and functional analysis, we identify the specific set of historical mutations that recapitulate the evolution of GR's hormone specificity from an MR-like ancestor. These substitutions repositioned crucial residues to create new receptor-ligand and intraprotein contacts. Strong epistatic interactions occur because one substitution changes the conformational position of another site. "Permissive" mutations—substitutions of no immediate consequence, which stabilize specific elements of the protein and allow it to tolerate subsequent function-switching changes—played a major role in determining GR's evolutionary trajectory.

A central goal in molecular evolution is to understand the mechanisms and dynamics by which changes in gene sequence generate shifts in function and therefore phenotype (*1*, *2*). A complete understanding of this process requires analysis of how changes in protein structure mediate the effects of mutations on function. Comparative analyses of extant proteins have provided indirect insights into the diversification of protein structure (*3*–*6*), and protein

engineering studies have elucidated structure-function relations that shape the evolutionary process (*7*–*11*). To directly identify the mechanisms by which historical mutations generated new functions, however, it is necessary to compare proteins through evolutionary time.

Here we report the empirical structures of an ancient protein, which we "resurrected" (*12*) by phylogenetically determining its maximum likelihood sequence from a large database of extant sequences, biochemically synthesizing a gene coding for the inferred ancestral protein, expressing it in cultured cells, and determining the protein's structure by x-ray crystallography. Specifically, we investigated the mechanistic basis for the functional evolution of the glucocorticoid receptor (GR), a hormone-regulated transcription factor present in all jawed vertebrates (*13*). GR and its sister gene, the mineralocorticoid receptor (MR), descend from the duplication of a single ancient gene, the ancestral corticoid receptor (AncCR), deep in the vertebrate lineage ~450 million years ago (Ma) (Fig. 1A) (*13*). GR is activated by the adrenal steroid cortisol and regulates stress response, glucose homeostasis, and other functions (*14*). MR is activated by aldosterone in tetrapods and by deoxycorticosterone (DOC) in teleosts to control electrolyte homeostasis, kidney and colon function, and other processes (*14*). MR is also sensitive to cortisol, though considerably less so than to aldosterone and DOC (*13*, *15*). Previously, AncCR was resurrected and found to have MR-like sensitivity to aldosterone, DOC, and cortisol, indicating that GR's cortisol specificity is evolutionarily derived (*13*).

To identify the structural mechanisms by which GR evolved this new function, we used x-ray crystallography to determine the structures of the resurrected AncCR ligand-binding domain (LBD) in complex with aldosterone, DOC, and cortisol (*16*) at 1.9, 2.0, and 2.4 Å resolution, respectively (table S1). All structures adopt the classic active conformation for nuclear receptors (*17*), with unambiguous electron density for each hormone (Fig. 1B and figs. S1 and S2). AncCR's structure is extremely similar to the human MR [root mean square deviation (RMSD) = 0.9 Å for all backbone atoms] and, to a lesser extent, to the human GR (RMSD = 1.2 Å). The network of hydrogen-bonds supporting activation in the human MR (*18*) is present in AncCR, indicating that MR's structural mode of action has been conserved for >400 million years (fig. S3).

Because aldosterone evolved only in the tetrapods, tens of millions of years after AncCR, that receptor's sensitivity to aldosterone was surprising (*13*). The AncCR-ligand structures indicate that the receptor's ancient response to aldosterone was a structural by-product of its sensitivity to DOC, the likely ancestral ligand, which it binds almost identically (Fig. 1C). Key contacts for binding DOC involve conserved surfaces among the hormones, and no obligate contacts are made with moieties at C11, C17, and C18, the only variable positions among the three hormones. These inferences are robust to uncertainty in the sequence reconstruction: We modeled each plausible alternate reconstruction [posterior probability (PP) > 0.20] into the AncCR crystal structures and found that none significantly affected the backbone conformation or ligand interactions. The receptor, therefore, had the structural potential to be fortuitously activated by aldosterone when that hormone evolved tens of millions of years later, providing the mechanism for evolution of the MR-aldosterone partnership by molecular exploitation, as described (*13*).

To determine how GR's preference for cortisol evolved, we identified substitutions that occurred during the same period as the shift in GR function. We used maximum likelihood phylogenetics to determine the sequences of ancestral receptors along the GR lineage (*16*). The reconstructions had strong support, with mean PP >0.93 and the vast majority of sites with PP >0.90 (tables S2 and S3). We synthesized a cDNA for each reconstructed LBD, expressed it in cultured cells, and experimentally characterized its hormone sensitivity in a reporter gene transcription assay (*16*). GR from the common ancestor of all jawed vertebrates (AncGR1 in Fig. 1A) retained AncCR's sensitivity to aldosterone, DOC, and cortisol. At the next node, however, GR from the common ancestor of bony vertebrates (AncGR2) had a phenotype like that of modern GRs, responding only to cortisol. This inference is robust to reconstruction uncertainty: We introduced

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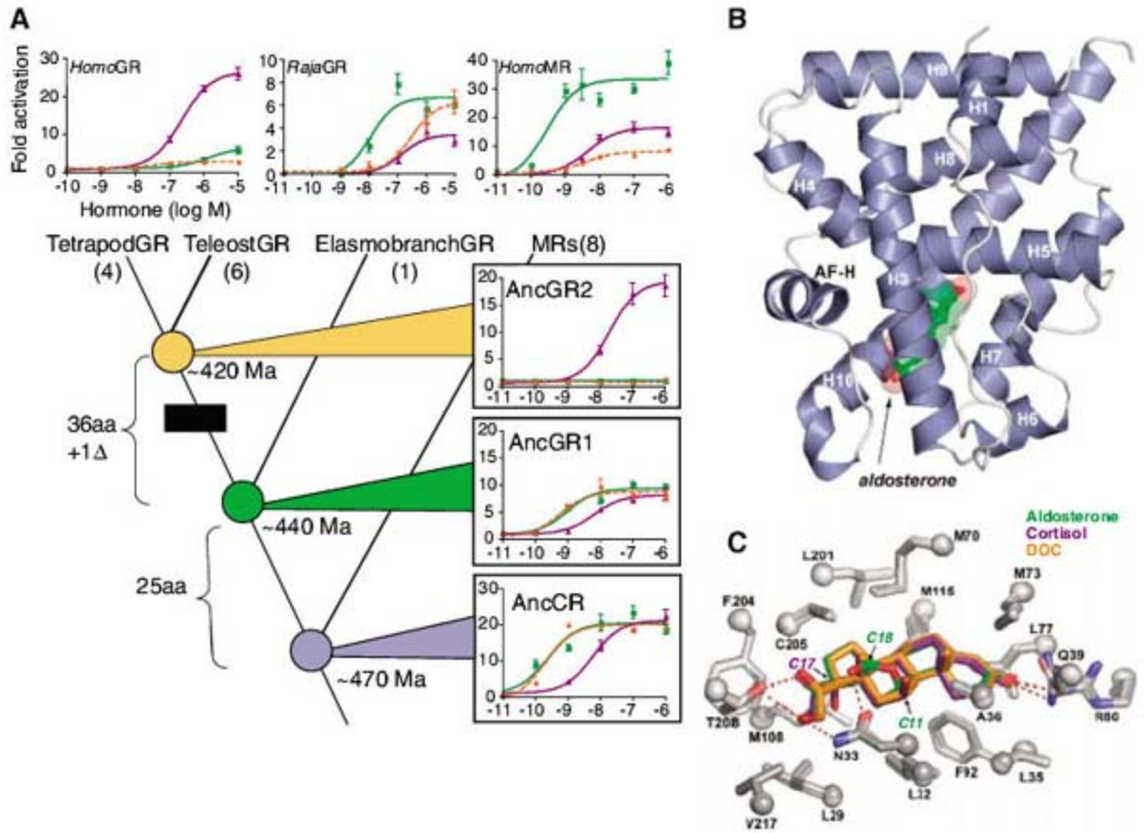


Fig. 1. (**A**) Functional evolution of corticosteroid receptors. Dose-response curves show transcription of a luciferase reporter gene by extant and resurrected ancestral receptors with varying doses (in log M) of aldosterone (green), DOC (orange), and cortisol (purple). Black box indicates evolution of cortisol specificity. The number of sequence changes on each branch is shown (aa, replacement; Δ, deletion). Scale bars, SEM of three replicates. Node dates from the fossil record (*19*, *20*). For complete phylogeny and sequences, see fig. S10 and table S5. (**B**) Crystal structure of the AncCR LBD with bound aldosterone (green, with red oxygens). Helices are labeled. (**C**) AncCR's ligand-binding pocket. Side chains (<4.2 Å from bound ligand) are superimposed from crystal structures of AncCR with aldosterone (green), DOC (orange), and cortisol (purple). Oxygen and nitrogen atoms are red and blue, respectively; dashed lines indicate hydrogen bonds. Arrows show C11, C17, and C18 positions, which differ among the hormones.

plausible alternative states by mutagenesis, but none changed function (fig. S4). GR's specificity therefore evolved during the interval between these two speciation events, ~420 to 440 Ma (*19*, *20*).

During this interval, there were 36 substitutions and one single-codon deletion (figs. S5 and S6). Four substitutions and the deletion are conserved in one state in all GRs that descend from AncGR2 and in another state in all receptors with the ancestral function. Two of these—S106P and L111Q (*21*)—were previously identified as increasing cortisol specificity when introduced into AncCR (*13*). We introduced these substitutions into AncGR1 and found that they recapitulate a large portion of the functional shift from AncGR1 to AncGR2, radically reducing aldosterone and DOC response while maintaining moderate sensitivity to cortisol (Fig. 2A); the concentrations required for half-maximal activation (EC_{50}) by aldosterone and DOC increased by 169- and 57-fold, respectively, whereas that for cortisol increased only twofold. A strong epistatic interaction between substitutions was apparent: L111Q alone had little effect on sensitivity to any hormone, but S106P dramatically reduced activation by all ligands. Only the combination switched receptor preference from aldosterone and DOC to cortisol. Introducing these historical substitutions into the human MR yielded a completely nonfunctional receptor, as did reversing them in the human GR (fig. S7). These results emphasize the importance of having the ancestral sequence to reveal the functional impacts of historical substitutions.

To determine the mechanism by which these two substitutions shift function, we compared the structures of AncGR1 and AncGR2, which were generated by homology modeling and energy minimization based on the AncCR and human GR crystal structures, respectively (*16*). These structures are robust to uncertainty in the reconstruction: Modeling plausible alternate states did not significantly alter backbone conformation, interactions with ligand, or intraprotein interactions. The major structural difference between AncGR1 and AncGR2 involves helix 7 and the loop preceding it, which contain S106P and L111Q and form part of the ligand pocket (Fig. 2B and fig. S8). In AncGR1 and AncCR, the loop's position is stabilized by a hydrogen bond between Ser^{106} and the backbone carbonyl of Met^{103}. Replacing Ser^{106} with proline in the derived GRs breaks this bond and introduces a sharp kink into the backbone, which pulls the loop downward, repositioning and partially unwinding helix 7. By destabilizing this crucial region of the receptor, S106P impairs activation by all ligands. The movement of helix 7, however, also dramatically repositions site 111, bringing it close to the ligand. In this conformational background, L111Q generates a hydrogen bond with cortisol's C17-hydroxyl, stabilizing the receptor-hormone complex. Aldosterone and DOC lack this hydroxyl, so the new bond is cortisol-specific. The net effect of these two substitutions is to destabilize the receptor complex with aldosterone or DOC and restore stability in a cortisol-specific fashion, switching AncGR2's preference to that hormone. We call this mode of structural evolution conformational epistasis, because one substitution remodels the protein backbone and repositions a second site, changing the functional effect of substitution at the latter.

Although S106P and L111Q ("group X" for convenience) recapitulate the evolutionary switch in preference from aldosterone to cortisol, the receptor retains some sensitivity to MR's ligands, unlike AncGR2 and extant GRs. We hypothesized that the other three strictly conserved changes that occurred between AncGR1 and AncGR2 (L29M, F98I, and deletion S212Δ) would complete the functional switch. Surprisingly, introducing these "group Y" changes into the AncGR1 and AncGR1 + X backgrounds produced completely nonfunctional receptors that cannot activate transcription, even in the presence of high ligand concentrations (Fig. 3A). Additional epistatic substitutions must have modulated the effect of group Y, which provided a permissive background for their evolution that was not yet present in AncGR1.

The AncCR crystal structure allowed us to identify these permissive mutations by analyzing the effects of group Y substitutions (Fig. 3B). In all steroid receptors, transcriptional activity depends on the stability of an activation-function helix (AF-H), which is repositioned when the ligand binds, generating the interface for transcriptional coactivators. The stability of this orientation is determined by a network of interactions among three structural elements: the loop preceding AF-H, the ligand, and helix 3 (*17*). Group Y substitutions compromise activation because they disrupt this network. S212Δ eliminates a hydrogen bond that directly stabilizes the AF-H loop, and L29M on helix 3 creates a steric clash and unfavorable interactions with the D-ring of the hormone. F98I opens up space between helix 3, helix 7, and the ligand; the resulting instability is transmitted indirectly to AF-H, impairing activation by all ligands (Fig. 3B). If the protein could tolerate group Y, however, the structures predict that these mutations would enhance cortisol specificity: L29M forms a hydrogen bond with cortisol's unique C17-hydroxyl, and the additional space created by F98I relieves a steric clash between the repositioned loop and Met^{108}, stabilizing the key interaction between Q111 and the C17-hydroxyl (Fig. 3B).

We hypothesized that historical substitutions that added stability to the regions destabilized by group Y might have permitted the evolving protein to tolerate group Y mutations and to complete the GR phenotype. Structural analysis suggested two candidates (group Z): N26T generates a new hydrogen bond between helix 3 and the AF-H loop, and Q105L allows helix 7 to pack more tightly against helix 3, stabilizing the latter and, indirectly, AF-H (Fig. 3B). As predicted, introducing group Z into the nonfunctional AncGR1 + X + Y receptor restored transcriptional activity, indicating that Z is permissive for Y (Fig. 3A). Further, AncGR1 + X + Y + Z displays a fully GR-like phenotype that is unresponsive to aldosterone and DOC and maintains moderate

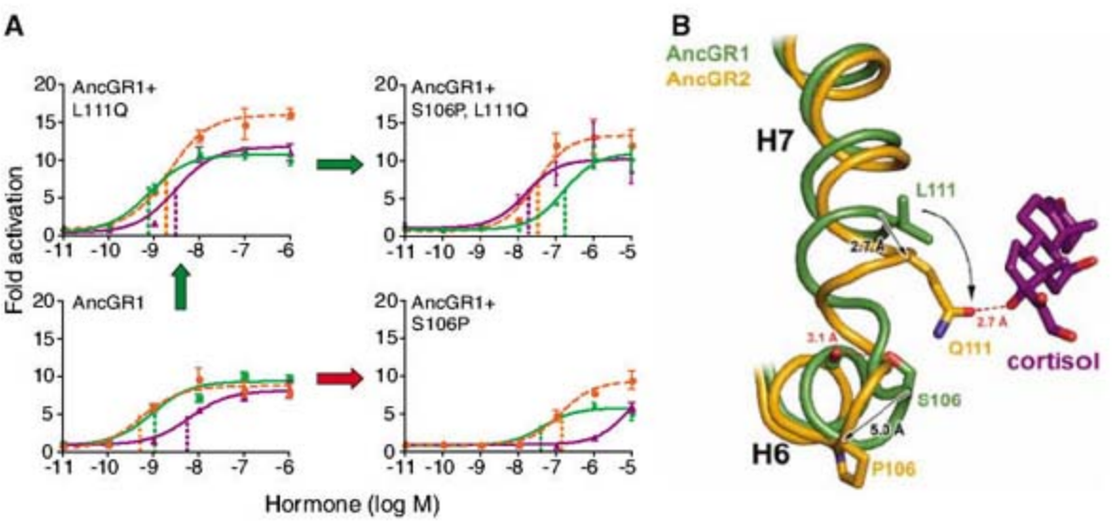


Fig. 2. Mechanism for switching AncGR1's ligand preference from aldosterone to cortisol. **(A)** Effect of substitutions S106P and L111Q on the resurrected AncGR1's response to hormones. Dashed lines indicate sensitivity to aldosterone (green), cortisol (purple), and DOC (orange) as the EC_{50} for reporter gene activation. Green arrow shows probable pathway through a functional intermediate; red arrow, intermediate with radically reduced sensitivity to all hormones. **(B)** Structural change conferring new ligand specificity. Backbones of helices 6 and 7 from AncGR1 (green) and AncGR2 (yellow) in complex with cortisol are superimposed. Substitution S106P induces a kink in the interhelical loop of AncGR2, repositioning sites 106 and 111 (arrows). In this background, L111Q forms a new hydrogen bond with cortisol's unique C17-hydroxyl (dotted red line).

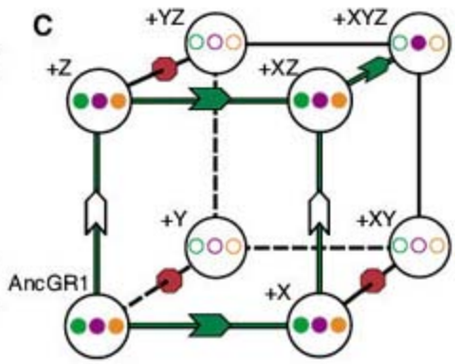
cortisol sensitivity. Both N26T and Q105L are required for this effect (table S4). Strong epistasis is again apparent: Adding group Z substitutions in the absence of Y has little or no effect on ligand-activated transcription, presumably because the receptor has not yet been destabilized (Fig. 3A). Evolutionary trajectories that pass through functional intermediates are more likely than those involving nonfunctional steps (*22*), so the only historically likely pathways to AncGR2 are those in which the permissive substitutions of group Z and the large-effect mutations of group X occurred before group Y was complete (Fig. 3C).

Our discovery of permissive substitutions in the AncGR1-AncGR2 interval suggested that other permissive mutations might have evolved even earlier. We used the structures to predict whether any of the 25 substitutions between AncCR and AncGR1 (fig. S5) might be required for the receptor to tolerate the substitutions that later yielded GR function. Only one was predicted to be important: Y27R, which is conserved in all GRs, stabilizes helix 3 and the ligand pocket by forming a cation-π interaction with Tyr^{17} (Fig. 4A). When we reversed Y27R in the GR-like AncGR1 + X + Y + Z, activation by all ligands was indeed abolished (Fig. 4B). In contrast, introducing Y27R into AncCR (Fig. 4B) or AncGR1 (fig. S9) had negligible effect on the receptor's response to any hormone. By conferring increased stability on a crucial part of the receptor, Y27R created a permissive sequence environment for substitutions that, millions of years later, remodeled the protein and yielded a new function.

These results shed light on long-standing issues in evolutionary genetics. One classic question is whether adaptation proceeds by mutations of large or small effect (*23*). Our findings are consistent with a model of adaptation in which large-effect mutations move a protein from one sequence optimum

A

Receptor	Hormone sensitivity (EC_{50},nM)		
	Aldosterone	Cortisol	DOC
AncGR1	1.0 (0.5,1.7)	6.4 (5.0,8.3)	0.5 (0.3,1.0)
AncGR1 + X	161.0 (119.2,217.4)	16.0 (8.0,31.9)	30.1 (17.9,50.7)
AncGR1 + Y	-	-	-
AncGR1 + XY	-	-	-
AncGR1 + Z	0.5 (0.2,1.4)	6.7 (4.5,10.0)	0.3 (0.1,0.7)
AncGR1 + XZ	200.0 (174.4,228.6)	2.9 (1.5,5.7)	22.4 (11.2,44.7)
AncGR1 + YZ	-	-	657.7 (491.1,880.7)
AncGR1 + XYZ	-	308.3 (135.7,700.5)	-



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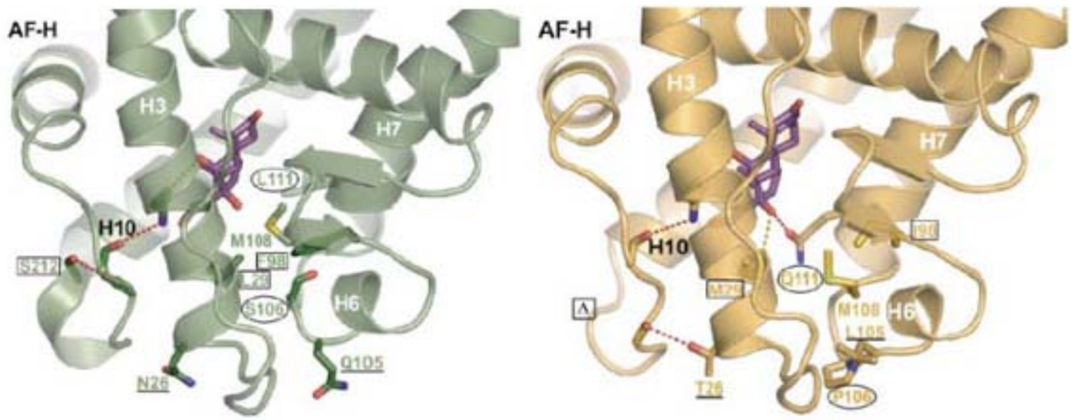
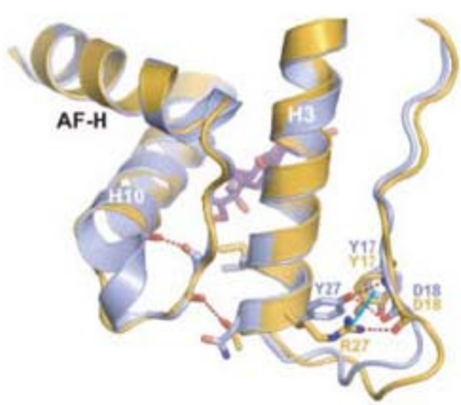


Fig. 3. Permissive substitutions in the evolution of receptor specificity. **(A)** Effects of various combinations of historical substitutions on AncGR1's transcriptional activity and hormone-sensitivity in a reporter gene assay. Group Y (L29M, F98I, and S212Δ) abolishes receptor activity unless groups X (S106P, L111Q) and Z (N26T and Q105L) are present; the XYZ combination yields complete cortisol-specificity. The 95% confidence interval for each EC_{50} is in parentheses. Dash, no activation. **(B)** Structural prediction of permissive substitutions. Models of AncGR1 (green) and AncGR2 (yellow) are shown with cortisol. Group X and Y substitutions (circles and rectangles) yield new interactions with the C17-hydroxyl of cortisol (purple) but destabilize receptor regions required for activation. Group Z (underlined) imparts additional stability to the destabilized regions. **(C)** Restricted evolutionary paths through sequence space. The corners of the cube represent states for residue sets X, Y, and Z. Edges represent pathways from the ancestral sequence (AncGR1) to the cortisol-specific combination (+XYZ). Filled circles at vertices show sensitivity to aldosterone (green), DOC (orange), and cortisol (purple); empty circles, no activation. Red octagons, paths through nonfunctional intermediates; arrows, paths through functional intermediates with no change (white) or switched ligand preference (green).

A



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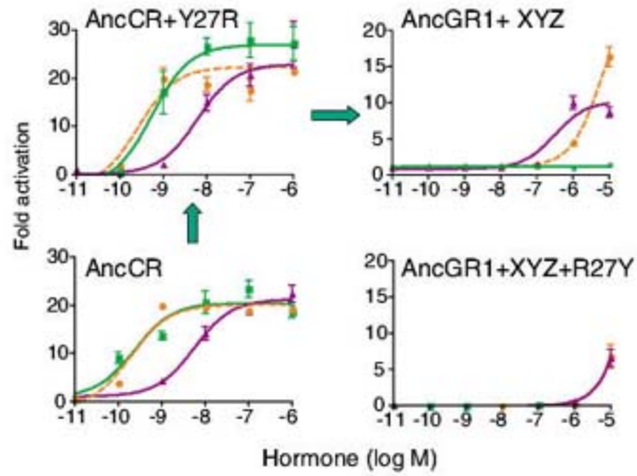

Fig. 4. Structural identification of an ancient permissive substitution. **(A)** Comparison of the structures of AncCR (blue) and AncGR2 (yellow). Y27R generates a novel cation-π interaction in AncGR2 (dotted cyan line), replacing the weaker ancestral hydrogen bond (dotted red) and imparting additional stability to helix 3. **(B)** Y27R is permissive for the substitutions that confer GR function. Reporter gene activation by AncGR1 + XYZ (upper right) is abolished when Y27R is reversed (lower right). (Left) Y27R has negligible effect in the AncCR background (or in AncGR1, fig. S9). Green, orange, and purple lines show aldosterone, DOC, and cortisol responses, respectively. Green arrows, likely pathway through functional intermediates.

to the region of a different function, which smaller-effect substitutions then fine-tune (*24*, *25*); permissive substitutions of small immediate effect, however, precede this process. The intrinsic difficulty of identifying mutations of small effect creates an ascertainment bias in favor of large-effect mutations; the ancestral structures allowed us isolate key combinations of small-effect substitutions from a large set of historical possibilities.

A second contentious issue is whether epistasis makes evolutionary histories contingent on chance events (*26*, *27*). We found several examples of strong epistasis, where substitutions that have very weak effects in isolation are required for the protein to tolerate subsequent mutations that yield a new function. Such permissive mutations create "ridges" connecting functional sequence combinations and narrow the range of selectively accessible pathways, making evolution more predictable (*28*). Whether a ridge is followed, however, may not be a deterministic outcome. If there are few potentially permissive substitutions and these are nearly neutral, then whether they will occur is largely a matter of chance. If the historical "tape of life" could be played again (*29*), the required permissive changes might not happen, and a ridge leading to a new function could become an evolutionary road not taken.

Our results provide insights into the structural mechanisms of epistasis and the historical evolution of new functions. GR's functional specificity evolved by substitutions that destabilized the receptor structure with all hormones but compensated with novel interactions specific to the new ligand. Compensatory mutations have been thought to occur when a second substitution restores a lost molecular interaction (*30*). Our findings support this notion, but in a reversed order: Permissive substitutions stabilized specific structural elements, allowing them to tolerate later destabilizing mutations that conferred a new function (*9*, *10*, *31*). We also observed a more striking mechanism: conformational epistasis, by which one substitution repositions another residue in three-dimensional space and changes the effects of mutations at that site. It is well known that mutations may have nonadditive effects on protein stability (*32*), and fitness (*9*, *33*), but we are aware of few cases (*11*, *34*) specifically documenting new functions or epistasis via conformational remodeling. This may be due to the lack of ancestral structures, which allow evolutionary shifts in the position of specific residues to be determined. Conformational epistasis may be an important theme in structural evolution, playing a role in many cases where new gene functions evolve via novel molecular interactions.

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Supporting Online Material

www.sciencemag.org/cgi/content/full/1142819/DC1
Materials and Methods
Figs. S1 to S10
Tables S1 to S5
References

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A Common Fold Mediates Vertebrate Defense and Bacterial Attack

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Proteins containing membrane attack complex/perforin (MACPF) domains play important roles in vertebrate immunity, embryonic development, and neural-cell migration. In vertebrates, the ninth component of complement and perforin form oligomeric pores that lyse bacteria and kill virus-infected cells, respectively. However, the mechanism of MACPF function is unknown. We determined the crystal structure of a bacterial MACPF protein, Plu-MACPF from *Photorhabdus luminescens*, to 2.0 angstrom resolution. The MACPF domain reveals structural similarity with pore-forming cholesterol-dependent cytolysins (CDCs) from Gram-positive bacteria. This suggests that lytic MACPF proteins may use a CDC-like mechanism to form pores and disrupt cell membranes. Sequence similarity between bacterial and vertebrate MACPF domains suggests that the fold of the CDCs, a family of proteins important for bacterial pathogenesis, is probably used by vertebrates for defense against infection.

The membrane attack complex/perforin (MACPF) domain was originally identified and named as being common to five complement proteins (C6, C7, C8α, C8β, and C9) and perforin (*1*–*3*) (fig. S1). These molecules perform critical functions in innate and

adaptive immunity. Despite limited sequence similarity between their MACPF domains, both perforin and C9 oligomerize and form pores that cause cell lysis (*1*). Complement factors C6 to C9 assemble to form a scaffold [the membrane attack complex (MAC)] that permits C9 polymerization into pores that lyse Gram-negative pathogens. Perforin is delivered by natural killer cells and cytotoxic T lymphocytes and forms oligomeric pores (12 to 18 monomers) in the plasma membrane of either virus-infected or transformed cells (*4*–*7*). Studies on these molecules have shown that the MACPF domain oligomerizes, undergoes conformational change, and is required for lytic activity (*8*, *9*).

Position-Specific Iterated (PSI)–BLAST searches (*10*, *11*) using the sequence of MACPF domains identify >500 proteins with significant expect scores. In addition to proteins involved in invasion and defense (*12*, *13*), family members include nonlytic proteins such as Astrotactin (*14*) (neural migration) and *Drosophila* Torso-like protein (*15*) (embryonic development). Functionally uncharacterized MACPF proteins are also evident in pathogenic bacteria such as *Chlamydia* spp. (*11*) and *Photorhabdus luminescens* (fig. S2). The MACPF family shares 15 to 20% sequence identity within the MACPF domain, and all members include the signature motif Y/W-G-T/S-H-F/Y-X_6-GG, where X is any amino acid (*11*, *16*) (fig. S2).

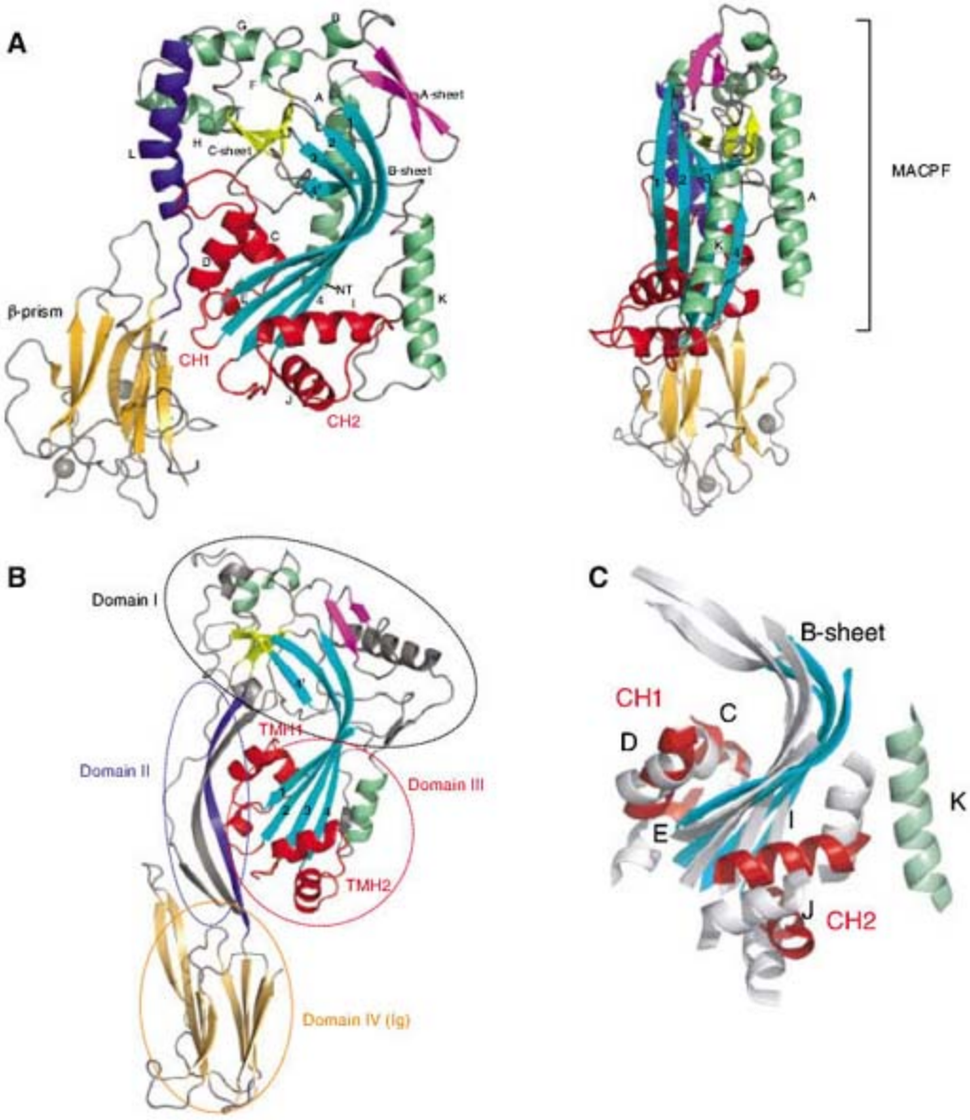

Fig. 1. The structure of Plu-MACPF. (**A**) Secondary-structure elements are labeled (see also fig. S2); CH1 and CH2 are shown in red. Two Cα atoms are shown as gray spheres, and the numbers represent the strand numbering of the B sheet. (**B**) Structure of PFO (*19*). Core elements of secondary structure common to both MACPF and CDCs are colored accordingly. In PFO, the region equivalent to the C sheet in MACPF is continuous with the light blue sheet and is shown in yellow. The first strand of the light blue sheet is shortened and at the top of the sheet, and the region in PFO equivalent to the A sheet (magenta) has collapsed over to form β-sheet hydrogen bonding with the second strand of the light blue sheet. (**C**) Stereo view of the superposition of the core of MACPF and PFO.

We targeted MACPF proteins for structural studies (*17*). Only one of these proteins, Plu-MACPF from *P. luminescens*, expressed solubly and yielded crystals (table S1). Although Plu-MACPF binds to the surface of insect cells (fig. S3), it is nonlytic under a range of conditions (see supporting online material data). However, the structure of its MACPF domain was expected to provide broad insight into the structure and mechanism of function of the MACPF superfamily.

The 2.0 Å crystal structure of Plu-MACPF shows that the 507 residues are divided into an N-terminal MACPF domain and a C-terminal β-prism type I domain (Fig. 1A and fig. S4A). The MACPF domain is a flat box-shaped molecule, featuring a ~50 Å four-stranded antiparallel β sheet (the B sheet) that contains a ~90° twist at strands s4B and s4′B. Two small clusters of α helices [cluster of helices-1 (CH1) and CH2] are packed on each side of the base of the B sheet and form much of the bottom half of the domain (Fig. 1A). The top of the MACPF domain comprises the two-stranded A sheet, the C sheet, and four short α helices (B and F to H). The β-prism domain is underneath CH1 and CH2 and comprises three antiparallel β sheets approximately related by a threefold axis. The β-prism fold is associated with membrane interaction (*18*); however, sequence searching revealed that it is not found in other members of the MACPF superfamily.

Structural characteristics of the MACPF domain, such as its flattened shape and twisted L-shaped central β sheet, bear a striking resemblance to the cholesterol-dependent cytolysin (CDC) family of toxins (*19*). Superpositions and topology diagrams (Fig. 1 and fig. S4) confirmed that the MACPF domain and domains I, II, and III of the archetypal CDC perfringolysin O (PFO) from *Clostridium perfringens* share a common core fold [root mean square (rms) deviation of 3.8 Å per atom over 361 Cα atoms]. The central β sheet, as well as the two clusters of α helices that switch to a membrane-spanning β conformation in PFO [transmembrane β

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hairpin 1 (TMH1) and TMH2, which correspond to CH1 and CH2, respectively, in MACPF], are conserved between the two structures (rms deviation of 0.9 Å per atom over 59 Cα atoms). Only three conserved residues in MACPF (G209, G270, and G271) (fig. S2) are also conserved in the CDC superfamily (equivalent residues in PFO: G274, G324, and G325) (*19*), which explains why PSI-BLAST searches using the MACPF sequences do not identify members of the CDC family with significant expect scores. The N- and C-terminal regions that flank the conserved core, which in PFO correspond largely to the noncontiguous linker domain II, are substantially different. Rather than a single α helix (L helix), the linker in PFO is composed of a twisted β strand supported by an elongated β hairpin derived from the N terminus (Fig. 1B and fig. S4). Despite these differences, the similarity of a complex core fold, together with functional similarities (*20*), suggests that MACPF domains and CDCs are homologous. We therefore propose that lytic MACPF proteins use a CDC-like mechanism of oligomerization and membrane insertion.

CDC-producing Gram-positive pathogens cause mortality in humans. In addition to PFO, well-characterized CDCs include pneumolysin (*Streptococcus pneumoniae*) and streptolysin O (*Streptococcus pyogenes*) (*21*). Like C9 and perforin, CDCs oligomerize, undergo conformational change, and insert into membranes to form doughnut-shaped pores (*22*). The molecular mechanism of pore formation of PFO and pneumolysin is well understood, involving ~30 molecules assembling via the flat faces of the globular head into a pre-pore oligomer that binds the cell membrane via the base of the C-terminal immunoglobulin domain (*19*, *21*–*24*). A conformational change results in the helical clusters TMH1 and TMH2 of each CDC unravelling to form two elongated amphipathic β hairpins that span the membrane (fig. S5). This converts the pre-pore into a giant β-barrel–lined channel (*19*, *21*–*24*). Although the amphipathic pattern of amino acids in TMH2 in PFO is imperfect (fig. S6), fluorescence and electron microscopy data reveal that this region is nonetheless able to insert into membranes (*24*). An analysis of the sequence of C9 and perforin also reveals an alternating pattern of hydrophobic and hydrophilic residues in CH1 and CH2, similar to that seen in TMH1 and TMH2 of CDCs and consistent with the ability to form an amphipathic membrane-spanning β hairpin (Fig. 1 and fig. S6). Together with the structural similarity, these data suggest that, rather than using two amphipathic α helices as originally proposed (*25*), lytic MACPF proteins span membranes using amphipathic β strands derived from CH1 and CH2.

Like TMH1 and TMH2 in CDCs, the sequence of CH1 and CH2 represents the most variable region of the superfamily, providing an exception to the general rule that functional elements tend to be highly conserved (*4*, *19*). An analysis of the patterns of conservation in MACPF reveals that the MACPF signature motif Y/W-G-T/S-H-F/Y, originally proposed to form one of two predicted membrane-spanning α helices (*25*), lies at the interface between CH1 and the body of the molecule (Figs. 2 and 3A and table S2). In CDCs, this region undergoes conformational change to allow TMH1 to unfurl (*19*, *22*–*24*). Another cluster of conserved residues centers on the sharp bend in the B sheet and includes four G residues (G209, G210, G270, and G271) that are >95% conserved in all MACPF proteins (Figs. 2 and 3B). In CDCs, three of these G residues are conserved (G274, G324, and G325 in PFO) and function as a hinge that allows sheet straightening during "hole punching" (*19*, *22*–*24*). We suggest that these

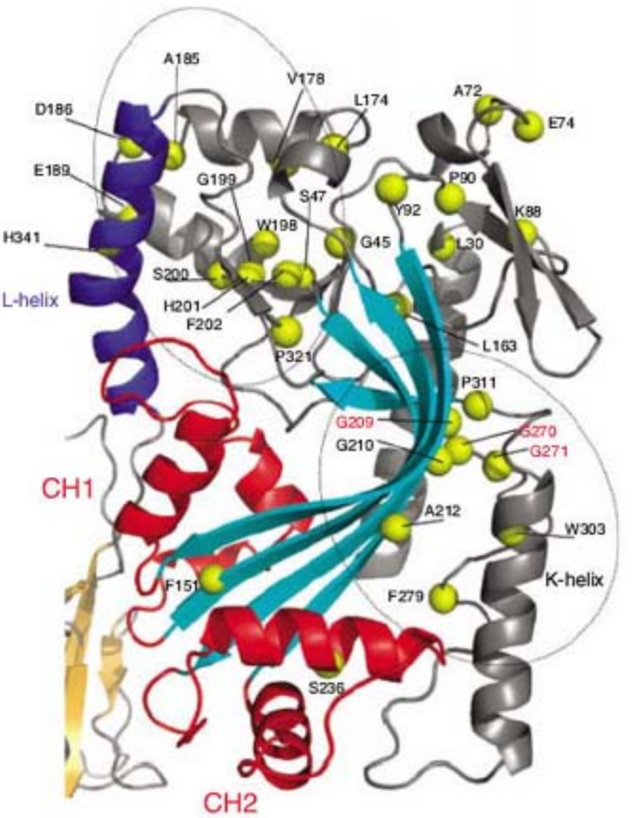

Fig. 2. Sequence conservation in the MACPF domain. Conserved residues in the MACPF family mapped onto the structure of Plu-MACPF (table S2). Three G residues (G209, G270, and G271) are also conserved in CDCs (red text). Two highly conserved clusters are circled, and the numbering is for Plu-MACPF.

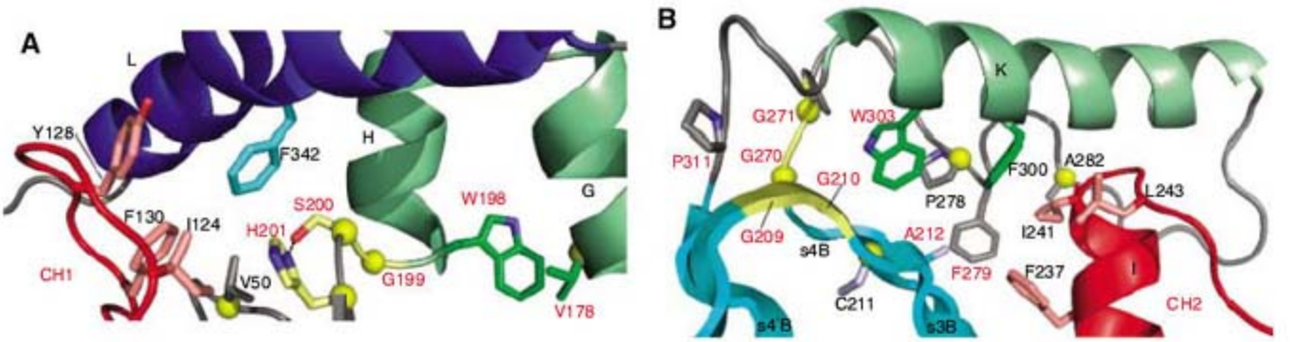

Fig. 3. Atomic interactions made by highly conserved residues. Interactions around (**A**) the conserved signature motif Y/W-G-T/S-H-F/Y and (**B**) the bend in the B sheet. In both panels, red labels indicate conserved residues, and yellow spheres on the Cα position indicate residues that are mutated in FHL. The numbering in both panels is for Plu-MACPF.

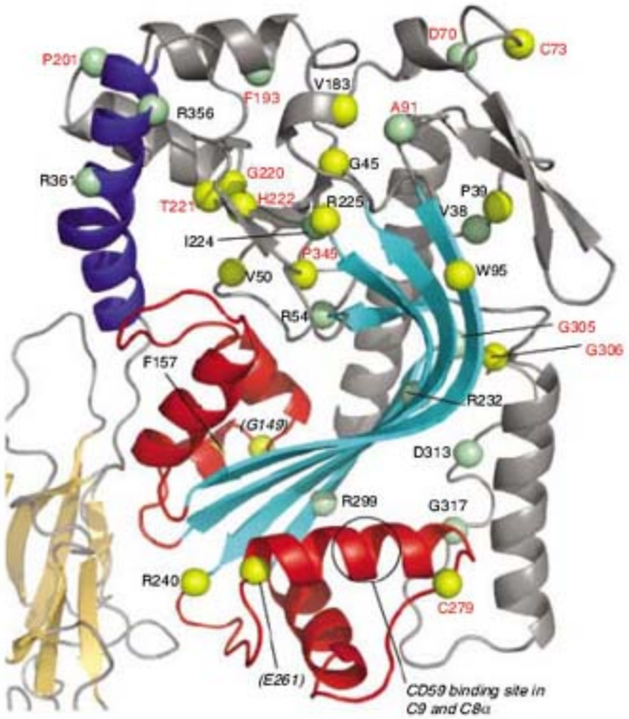

Fig. 4. Position of disease-linked mutations in perforin. The positions of mutations in perforin that cause early onset FHL (yellow) and late onset atypical FHL (pale green) are shown by spheres (table S2). The numbering is for perforin, and red text indicates a mutation of a conserved residue (table S2). The positions of G149 and E261 in perforin are approximate, because these are insertions relative to Plu-MACPF. The position of the CD59 binding site in C9 and C8α is indicated by a black circle (*30*).

residues may permit a similar conformational change in the MACPF domain.

The structure of the MACPF domain gives us a better understanding of mutations in perforin that cause the rare immunological disorder familial hemophagocytic lymphohistiocytosis (FHL) (*4*). In addition to missense mutations of highly conserved residues (Figs. 3 and 4 and table S2), several perforin mutations map to CH1 and CH2 or their surrounding pockets, consistent with a functional role for these regions (Figs. 3 and 4). However, the most intriguing perforin variant identified to date is the A91V (Y92 in Plu-MACPF) polymorphism of perforin which occurs at a frequency of ~3 to 17% and is linked to misfolding, decreased lytic activity, and predisposition to late onset hemophagocytic lymphohistiocytosis (*4*, *26*–*28*). This variant maps to the s2A/s1B loop and its interface with the F helix (Fig. 4). Further, the dysfunctional variant V183G (168 in Plu-MACPF) maps to the F helix and is predicted to pack against A91 (Y92) (Fig. 4). Thus, perturbations of the s2A/s1B–F helix interface may underpin the perforin A91V misfolding phenotype.

Previous studies have shown that C9/MAC activity is controlled by host inhibitors such as CD59 that prevent unwanted cell lysis. Sequences on C9 and C8α that participate in CD59 binding (*29*, *30*) map to CH2 (Fig. 4). Thus, we suggest that CD59 may regulate MAC function by interfering with CH2.

The MACPF domain is commonly found to be associated with other N- and C-terminal modules (fig. S1) that probably control or target MACPF function. For example, the C-terminal C2 domain of perforin mediates initial interactions with membranes (*4*), an analogous role to that of domain IV of the CDCs (*19*).

Although Plu-MACPF appears to be nonlytic under the conditions tested, we cannot exclude the possibility that it requires a cofactor or specific receptor for function. On the other hand, certain MACPF proteins (e.g., C6, C7, C8β, and Astrotactin) do not lyse cells and instead perform other roles. We speculate that certain utilities of the MACPF fold, such as conformational flexibility and membrane insertion, may have been exploited for nonlytic purposes. Indeed, parallels can be drawn with the eukaryote B cell lymphoma 2 family of proteins that share a similar fold to bacterial colicin-like toxins but insert into membranes rather than lyse cells (*31*).

This work implies that lytic members of the MACPF superfamily use a CDC-like mechanism for membrane penetration and pore formation. Our findings suggest that the fold of the CDCs, a family of proteins that causes tissue destruction in human diseases, is used by vertebrates for defense against bacterial and viral infection.

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Supporting Online Material

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Materials and Methods
Figs. S1 to S6
Tables S1 and S2
References

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Structure of C8α-MACPF Reveals Mechanism of Membrane Attack in Complement Immune Defense

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Membrane attack is important for mammalian immune defense against invading microorganisms and infected host cells. Proteins of the complement membrane attack complex (MAC) and the protein perforin share a common MACPF domain that is responsible for membrane insertion and pore formation. We determined the crystal structure of the MACPF domain of complement component C8α at 2.5 angstrom resolution and show that it is structurally homologous to the bacterial, pore-forming, cholesterol-dependent cytolysins. The structure displays two regions that (in the bacterial cytolysins) refold into transmembrane β hairpins, forming the lining of a barrel pore. Local hydrophobicity explains why C8α is the first complement protein to insert into the membrane. The size of the MACPF domain is consistent with known C9 pore sizes. These data imply that these mammalian and bacterial cytolytic proteins share a common mechanism of membrane insertion.

Protection in blood against Gram-negative bacteria critically depends on the cytolytic activity of the terminal pathway of the complement system (*1*, *2*). Deficiency in components of the terminal pathway results in recurrent bacterial infections in humans [in particular, meningococcal infections (*3*)]. The terminal pathway is initiated when complement protein C5 is proteolytically activated into two fragments, C5a and C5b, in the complement cascade (*4*). C5b then sequentially binds C6, C7, C8, and multiple copies of C9, forming a C5b–9 complex called the MAC. The complement proteins C6 to C9 are homologous and have a central MACPF domain of molecular mass ~40 kD, flanked by small regulatory domains at the N and C termini (fig. S1) (*5*). C8 is a trimer made up of homologous proteins C8α and C8β, each of which contain a MACPF domain, and a lipocalin protein C8γ that is covalently linked to C8α through a disulfide bridge (*6*). During assembly of the MAC, C7 mediates the initial binding to the membrane surface. However, the C8α component of C8 is the first protein that traverses the lipid bilayer (*7*, *8*). C5b–8 complexes, obtained in the absence of C9, have hemolytic activity, indicating that C8 penetration leads to a loss of membrane integrity (*9*). After C5b–8 assembly, multiple C9 molecules bind and oligomerize into pores, consisting of 12 to 18 C9 monomers, that are 100 ± 10 Å wide and 160 Å high (*10*–*12*). Host cells are protected from this membrane attack by CD59, which binds to C8α and C9 during MAC assembly, preventing pore formation (*13*). Cytotoxic T lymphocytes and natural killer cells secrete granules containing perforin, which (like the complement proteins C6 to C9) has a central MACPF domain. Perforin multimerizes, forming similar pores composed of ~20 monomers (*14*–*16*). Perforin, however, does not use accessory proteins for membrane binding (*16*). The mechanism of membrane insertion and pore formation by these proteins of the immune system is unclear.

We expressed and crystallized the human C8α-MACPF domain (residues 103 to 462). The C8α-MACPF domain retains its ability to form heterotrimeric C8 (with full-length C8β and C8γ) that is functionally active in membrane attack and pore formation (*17*). The structure was determined to 2.5 Å resolution by experimental phasing (see the Materials and Methods, table S1, and fig. S2 in the supporting online material). The overall structure consists of a central kinked four-stranded β sheet surrounded by α helices and β strands, forming two structural segments (which we call d1 and d3 for reasons discussed below) (Fig. 1A). Overall, the molecule has a thin L-shaped appearance with dimensions 67 Å by 55 Å by 24 Å.

The observed fold of C8α-MACPF with its central kinked β sheet resembles the fold of domains d1 and d3 of intermedilysin and perfringolysin, which are cholesterol-dependent cytolysins (CDCs) secreted by the Gram-positive bacteria (*18*, *19*) (Fig. 1B and fig. S3). CDCs undergo substantial refolding of part of their structure in transforming from monomeric soluble proteins to multimeric membrane pores [reviewed in (*20*)]. CDCs are built up of four domains: d1 to d4. Domain d4 is responsible for membrane binding (*21*, *22*), whereas d2 forms a linker to d1 and d3, which mediate pore formation (*23*). Domains d1 and d3 correspond to the two halves of the kinked β sheet in the structure of C8α-MACPF, which is consistent with the membrane-insertion function of C8α-MACPF. The absence of the d2 and d4 domains in C8α-MACPF correlates, however, with marked topological differences in d1 (fig. S3, C and D). The modules flanking the C8α-MACPF domain [that is, the N-terminal thrombospondin type 1 (TSP1) and low-density lipoprotein receptor class a domains and the C-terminal epidermal growth factor–like and TSP1 domains] are linked on opposite sides to d1 (Fig. 1A). The covalent binding site for C8γ (Cys^{164}) is located in a disordered surface loop on the N-terminal side of d1. In contrast, the topologies of d3 in C8α and CDCs are very similar and are characterized by an antiparallel β sheet (strands β1 to β4) with extended, connecting regions β1-β2 and β3-β4.

Residues from domain d3 in CDCs form the wall of the β barrel pores. In CDCs, the antiparallel β sheet (strands β1 to β4) in d3 has two helical connections (between strands β1-β2 and β3-β4). By means of multiple spectroscopic methods, these two helical regions have been shown to refold into amphipathic β hairpins [denoted transmembrane β hairpin 1 (TMH1) and TMH2], which insert into the membrane, forming a β barrel pore (*24*, *25*). C8α-MACPF

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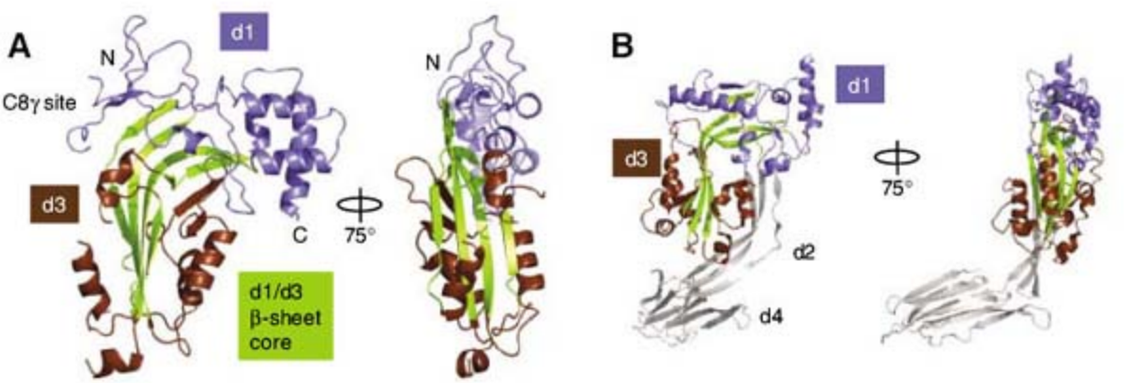


Fig. 1. Structure of human C8α-MACPF. Cα representation of C8α-MACPF (**A**) and intermedilysin (PDB accession code 1s3r) (**B**) in two views. The top and bottom halves of the molecule are denoted d1 (blue) and d3 (brown), respectively. The central kinked β sheet (part of both d1 and d3) is shown in green. The additional domains d2 and d4 in intermedilysin are shown in gray. Figures are produced with PyMOL (*30*).

exhibits similar, but longer, regions in between strands β1-β2 and β3-β4. The first region spans 58 residues (residues 201 to 258) and forms two α helices interspersed with a β hairpin (Fig. 2A). The second region consists of 62 residues (residues 326 to 387). This region has two discernible α helices in the electron density but is largely disordered. Like in CDCs, these regions show high sequence variation across species (fig. S4). In C8α, we observe a partitioning into three segments for these regions: (i) charged and amphipathic, (ii) hydrophobic, and (iii) charged and amphipathic (Fig. 2B and fig. S4). In the structure, the hydrophobic middle part (26 residues long) of region β1-β2 forms a β hairpin that aligns with the central sheet of d1. The corresponding part in region β3-β4 is 25 residues long and is delimited by the disulfide bond Cys^{345}-Cys^{369}. This hydrophobic part has three charged residues positioned halfway between the cysteine residues. The hydrophobic character of the central β1-β2 and β3-β4 parts is consistent with membrane insertion without pore formation, as expected for the function of C8. Presumably, the central β3-β4 part would traverse the membrane completely and position the three charged residues on the inside of the target membrane. In contrast, the central parts of the β1-β2 and β3-β4 regions in C9 and perforin (Fig. 2B and fig. S4) have an alternating hydrophobic and hydrophilic character (like the TMHs of CDCs). This amphipathic character is consistent with forming a β barrel pore with a hydrophilic inside and a hydrophobic outside that faces the lipid membrane. The flanking regions in C8α, C9, and perforin contain short stretches of consecutive charged residues indicative of a solvent-exposed character. We hypothesize that the central segments traverse the membrane (forming TMHs) and that the flanking parts protrude above the membrane.

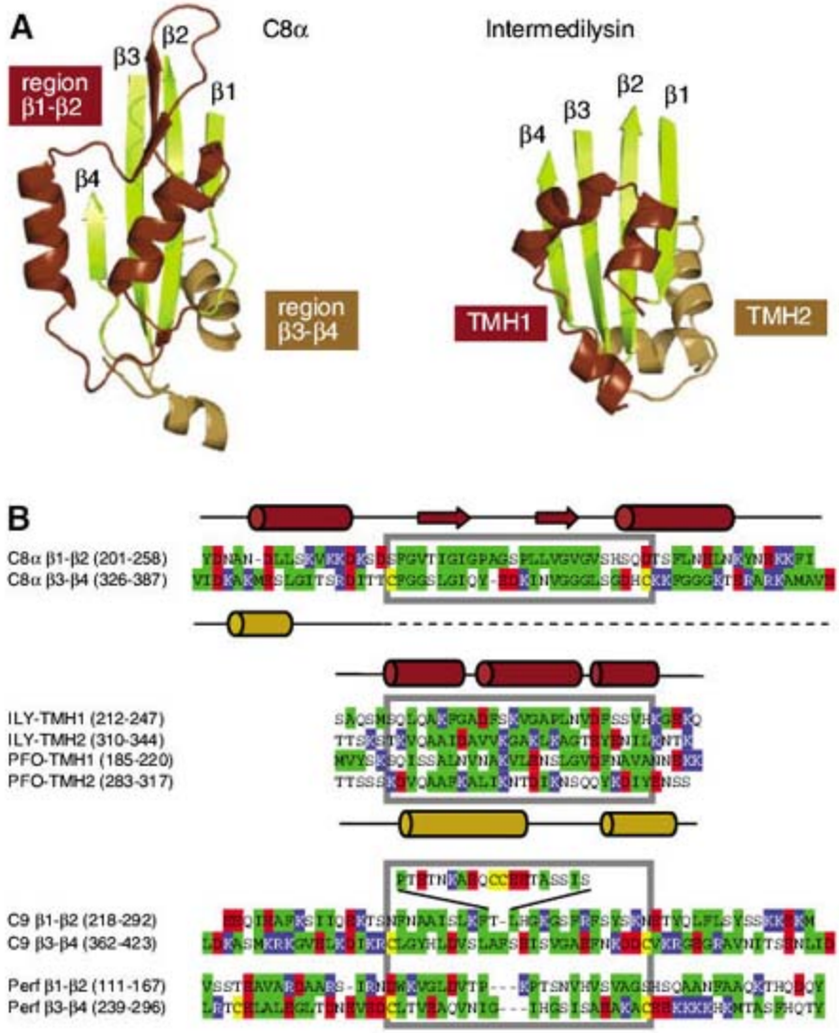
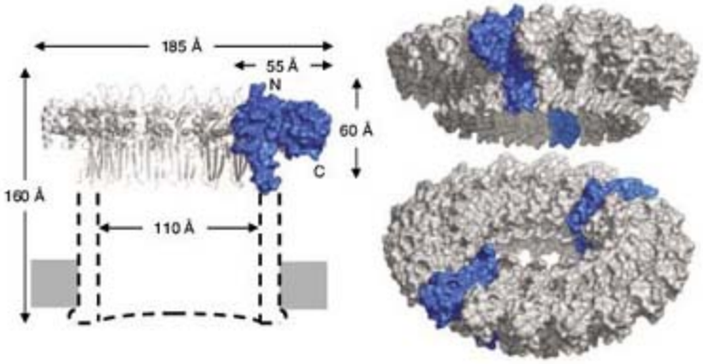


Fig. 2. Comparison of putative transmembrane regions. (**A**) Cartoon diagrams of domains d3 of C8α-MACPF (left) and intermedilysin (right). The putative β hairpin regions β1-β2 and TMH1 are colored in dark brown, and β3-β4 and TMH2 are colored in light brown. (**B**) Sequence alignment of (i) the β1-β2 and β3-β4 regions of C8α, C9, and perforin (Perf) and (ii) TMH1 and TMH2 of perfringolysin (PFO) and intermedilysin (ILY). Residues (*31*) are colored according to character: hydrophobic (green), positively charged (blue), negatively charged (red), and hydrophilic (white). Yellow indicates cysteine residues. Secondary structure elements, as observed for C8α-MACPF and intermedilysin, are indicated. Putative transmembrane regions are indicated by gray boxes.

Electron micrographs of the MAC and poly (C9) reveal a pore (~100 Å inner-diameter, ~160 Å height, and ~200 Å outer-diameter torus) and a small rim at the base of the pore (*12*). Our structure shows that a soluble, monomeric MACPF domain has a thin "L" shape. In analogy with CDCs, the β1-β2 and β3-β4 regions in d3 are expected to change into long β hairpins upon membrane insertion, contributing four strands per monomer. Extending 60 residues into one straight β hairpin yields a maximum length of ~100 Å; this structure would extend from the existing four-stranded β sheet in d3. Together with the MACPF domain, this yields a total length of ~160 Å, which is consistent with the height measured for MAC and C9 pores by electron microscopy (EM). Similarly, modeling of the x-ray structure of perfringolysin into a cryo-EM map of a pneumolysin pore also indicated extended β hairpins oriented parallel to the membrane normal (*26*). However, the β strands are most likely twisted and tilted (as observed in many β barrel structures of outer-membrane proteins); possibly, the missing N-terminal domains contribute to the height of the C9 pore. Furthermore, the putative TMH1 in C9 has a 17-residue extension, which is consistent with the presence of a small rim at the bottom side of the pore. Based on the MACPF domain of C8α, we constructed a hypothetical model of the C9 pore torus. Sixteen and 18 copies of the molecule were placed in rings, with the β1 to β4 strands of d3 placed on the inside (Fig. 3). This simplistic modeling resulted in rings with an inner diameter of 97 and 110 Å and an outer diameter of 170 and 185 Å, respectively. The inner diameters of these models are close to the observed 100 Å; the smaller outer diameter (170 to 185 Å versus 200 Å)

Fig. 3. Hypothetical model of the C9 pore. Shown is a pore model derived from a ring of 18 monomers of C8α-MACPF. (**Left**) Cross section of the pore, with MACPF domains forming the torus. (**Right**) Two orientations of the torus in surface representation, with two individual monomers highlighted (in blue) for convenience.



is possibly caused by the missing C-terminal domains that are connected to the outer rim of the torus. Thus, based on a MACPF domain, the main characteristics of the C9 pore can be modeled.

Membrane recognition and pore formation by the complement proteins depend on a sequential assembly of the MAC. The C8α-MACPF and C8β-MACPF domains are sufficient for a functional C5b–8 complex, indicating that the flanking N- and C-terminal domains in C8 are not essential for complex formation (*17*, *27*). The flanking domains, however, possibly cover the putative TMHs in soluble C8. Soluble forms of the cell-surface protein CD59 do not bind soluble C8 or C9 (*13*). CD59 binds residues 365 to 371 of C9 and residues 320 to 415 in C8α (*28*), which map to the TMH2 region. Presumably, docking of C8 or C9 onto the MAC reorients the flanking domains exposing the TMHs, which are subsequently "caught in the act" by CD59 present on host cells, and hence the membrane insertion is blocked. In CDCs, membrane insertion only takes place after oligomerization [that is, a large oligomeric prepore is formed on top of the membrane before the membrane is perforated (*26*)]. C8α inserts without oligomerization, which is consistent with the hydrophobic character of the putative TMHs. Partial and incomplete pores are observed, when limiting numbers of C9 are available for binding to C5b–8 (*11*). These data indicate that MAC pore formation is gradual and does not require oligomeric prepores. In this process, C8 plays an important role by binding to the membrane-bound C5b–7 complex, penetrating and destabilizing the membrane, thus readily enabling pore formation by C9.

Perforin, perhaps, acts more like CDCs. Membrane binding by perforin is Ca^{2+}-dependent and is mediated by its C-terminal C2 domain (*29*). The C2 fold is closely related to the fold of the C-terminal d4 domain in CDCs (fig. S5). Notably, the "undecapeptide" membrane–binding site in d4 overlaps with the Ca^{2+}-dependent binding site in C2, indicating a common orientation when bound to a membrane. Like in CDCs and C9, the putative TMHs of perforin are amphipathic in character. The amphipathic regions presumably do not penetrate the membrane easily. We argue that unassisted pore formation [as for CDCs, perforin, and in vitro poly(C9)] hence requires formation of a large oligomeric prepore on the membrane to facilitate perforation of the membrane.

The MACPF domain of complement proteins C6 to C9 and perforin is similar to domains d1 and d3 of bacterial CDCs. This finding indicates a possible common evolutionary origin and a common mechanism of membrane insertion. The structural insights could be valuable in the design of therapeutics preventing inappropriate activation of the terminal pathway of complement, as in the case of paroxysmal nocturnal hemoglobinuria and hyperacute rejection of transplanted organs.

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31. Single-letter abbreviations for the amino acid residues are as follows: A, Ala; C, Cys; D, Asp; E, Glu; F, Phe; G, Gly; H, His; I, Ile; K, Lys; L, Leu; M, Met; N, Asn; P, Pro; Q, Gln; R, Arg; S, Ser; T, Thr; V, Val; W, Trp; and Y, Tyr.

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Supporting Online Material

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Materials and Methods
Figs. S1 to S5
Table S1
References

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Anti-Inflammatory Activity of Human IgG4 Antibodies by Dynamic Fab Arm Exchange

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Antibodies play a central role in immunity by forming an interface with the innate immune system and, typically, mediate proinflammatory activity. We describe a novel posttranslational modification that leads to anti-inflammatory activity of antibodies of immunoglobulin G, isotype 4 (IgG4). IgG4 antibodies are dynamic molecules that exchange Fab arms by swapping a heavy chain and attached light chain (half-molecule) with a heavy-light chain pair from another molecule, which results in bispecific antibodies. Mutagenesis studies revealed that the third constant domain is critical for this activity. The impact of IgG4 Fab arm exchange was confirmed in vivo in a rhesus monkey model with experimental autoimmune myasthenia gravis. IgG4 Fab arm exchange is suggested to be an important biological mechanism that provides the basis for the anti-inflammatory activity attributed to IgG4 antibodies.

In the classic paradigm, immunoglobulins represent products of clonal B cell populations, each producing antibodies recognizing a single antigen specificity (*1*, *2*). Human immunoglobulin G (IgG) antibodies exist in four subclasses with distinct structural and functional properties. IgGs are composed of two heavy chain–light chain pairs (half-molecules), which are connected via inter–heavy chain disulfide bonds situated in the hinge region, as well as by noncovalent bonds mostly situated between the third constant (C_H3) domains (*3*). Stability of the inter–heavy chain disulfide bonds varies between subclasses, and for IgG4 in particular, intra–heavy chain disulfide bonds may be formed instead (*4*).

IgG4 antibodies differ functionally from other IgG subclasses in their anti-inflammatory activity, which includes a poor ability to induce complement and cell activation because of low affinity for C1q (the q fragment of the first component of complement) and Fc receptors (*5*, *6*).

Consequently, IgG4 has become the preferred subclass for immunotherapy, in which recruitment of host effector function is undesirable. Another, more poorly understood property of blood-derived IgG4 is its inability to cross-link identical antigens, which is referred to as "functional monovalency" (*7*, *8*). In contrast, cross-linking of nonidentical antigens (bispecificity) has been observed under certain conditions (*9*). It has been postulated that these observations might be explained by the exchange of half-molecules between distinct IgG4 molecules (*9*–*11*). This hypothesis, however, has not been widely accepted, as this exchange previously could not be confirmed using recombinant IgG4 antibodies (*9*). Here we show, using well-characterized monoclonal antibodies, that Fab arm exchange represents a general characteristic of IgG4.

We explored this issue using blood-derived and recombinant IgG4 antibodies against the major birch pollen (Betv1) and cat (Feld1) allergens (*12*). Serum from an allergic patient with high IgG4 titers against both antigens contained bispecific antibodies that cross-linked Betv1 and Feld1, whereas such reactivity was not detected in control sera (fig. S1). This peculiar bispecific reactivity of blood-derived IgG4 could not be reproduced by simple mixing in vitro (fig. S2), as previously observed for other antigens (*13*). To investigate whether bispecificity is the result of in vivo molecular processing, we injected an equal mixture of recombinant IgG4-Betv1 and IgG4-Feld1 or corresponding IgG1 controls into immunodeficient mice. Blood samples were drawn, after which we measured Feld1/Betv1-bispecific IgG (Fig. 1A). Interestingly, bispecific antibodies appeared in the blood of mice injected with IgG4, but not IgG1, mixtures. A stochastic Fab arm exchange between equal amounts of IgG4-Betv1 and IgG4-Feld1 would be consistent with approximately half of the IgG4 molecules acquiring bispecificity (*14*). To demonstrate the plasticity of this process, we injected an IgG4 mixture including a 20-fold excess of an additional IgG4 with irrelevant specificity, which almost abrogated Feld1/Betv1-bispecific reactivity (Fig. 1A). This inhibition is explained by the generation of bispecific IgG4 not detected in our Feld1-Betv1 cross-linking assay. If the observed bispecificity resulted from Fab arm exchange, then the increase in bispecific activity should be accompanied by an equivalent loss of monospecific cross-linking activity (*15*), which was indeed observed (fig. S3).

IgG molecules are protected from catabolism by the neonatal Fc receptor (FcRn) by an intracellular recycling route (*16*). However, FcRn was not required for Fab arm exchange because no differences in the generation of bispecific IgG4 were observed between wild-type and FcRn-deficient mice (fig. S4). This suggests that Fab arm exchange may occur in the extracellular milieu.

The molecular mechanisms for Fab arm exchange were studied by defining in vitro conditions. We found that bispecific IgG4, but not IgG1, molecules were generated on mixing with isolated blood cells, but not with human serum. Bispecific IgG4 molecules were generated in the presence of human erythrocytes with similar kinetics as observed in vivo (Fig. 2A). A low-molecular-weight compound from erythrocyte lysates appeared essential for the exchange reaction (table S1). This observation, in combination with the requirement for breaking inter–heavy chain disulfide bonds, prompted us to test whether bispecific IgG4 was generated in the presence of small reducing agents such as reduced glutathione (GSH). Notably, the addition of GSH or other reducing agents to a mixture of purified IgG4, but not IgG1, was sufficient to induce Fab arm exchange (Fig. 2B). The reaction in the presence of GSH occurred more efficiently at physiological than at low temperature (fig. S5).

We extended our analyses to fully human monoclonal antibodies (HumAbs) with a matched set of well-characterized recombinant human IgG1 and IgG4 antibodies directed against CD20 antigen and epidermal growth factor receptor (EGFR) [HumAbs 7D8 (*17*) and 2F8 (*18*), respectively]. Bispecificity was evaluated with a sandwich enzyme-linked immunosorbent assay (ELISA) consisting of recombinant EGFR immobilized on the solid phase and an anti-idiotype antibody against HumAb 7D8 as a detecting reagent. The kinetics of bispecific antibody formation against EGFR/CD20, which occurred only for the IgG4 mixture and only in the presence of GSH, is shown in Fig. 2C. The molecular requirements for Fab arm exchange were studied by mutagenesis. Unexpectedly, our experiments suggest that the C_H3 domain and not the core hinge is dominantly involved in the reaction. Thus, exchanging C_H3 domains between IgG1 and IgG4 activated Fab arm exchange for IgG1 and abrogated activity for IgG4 (Fig. 2D). In contrast, replacing the IgG1 core hinge sequence with the IgG4 sequence alone [by replacing Pro^{228} with Ser (P228S)] had no effect, and the IgG4 C_H3 sequence was additionally required for full Fab arm exchange activity by the IgG1 mutant (Fig. 2D).

To conclusively demonstrate that Fab arm exchange is indeed the result of an intermolecular exchange reaction, we analyzed the molecules generated using size-exclusion chromatography and mass spectrometry (MS). First, we performed size-exclusion analyses of plasma from two of the mice injected with an IgG4 antibody mixture. Bispecific antibodies eluted at the expected position for monomeric IgG, which ruled out the possibility that the observed reactivity was due to aggregation (fig. S6). Second, we incubated a mixture of IgG4-EGFr and IgG4-CD20 in the absence or presence of GSH, followed by mass spectrometry [electrospray ionization time-of-flight mass spectrometry (ESI-TOF MS)]. Figure 2E shows that the molecular masses of IgG4-CD20 (145.5 kD) and IgG4-EGFR (145.9 kD) remained unchanged in the absence of GSH. In the presence of GSH (Fig. 2F), however, a new peak with an intermediate mass appeared (145.7 kD). The novel mass corresponded to the expected mass of the bispecific antibody against EGFR/CD20 detected in Fig. 2C. Moreover, from the peak heights of the MS spectra it was estimated that the bispecific anti-

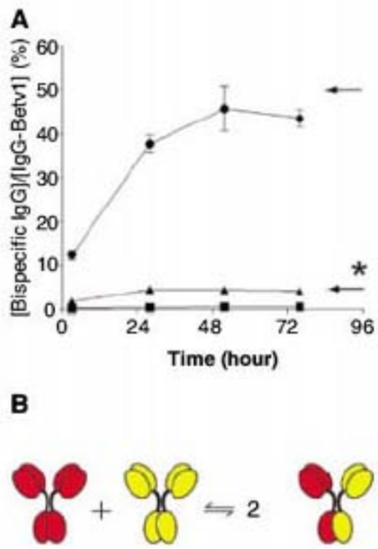

Fig. 1. Bispecific human IgG4 molecules are generated in vivo. **(A)** Groups (n = 5) of nude mice were injected with antibody mixtures: IgG1-Betv1/IgG1-Feld1 (squares), IgG4-Betv1/IgG4-Feld1 (circles), or IgG4-Betv1/IgG4-Feld1 + irrelevant recombinant IgG4 (IgG4-EGFR; triangles) (test antibodies, 100 μg each per mouse; irrelevant IgG4, 2000 μg per mouse). The generation of bispecific antibodies was followed by assessing Betv1 and Feld1 bispecific reactivity, which was expressed as a percentage relative to the total IgG-Betv1 concentration. The top arrow indicates the expected level of bispecific reactivity (50%) in mice receiving an equal amount of IgG4-Betv1 and IgG4-Feld1 (*14*); the bottom arrow with asterisk indicates the expected level of bispecific reactivity (4%) in the presence of excess irrelevant IgG4. Error bars represent SEM. **(B)** IgG4 Fab arm exchange occurs by the exchange of a heavy chain–light chain pair (half-molecule) of one IgG4 molecule with that of another IgG4 molecule. The IgG4 molecule may thereby acquire two distinct Fab arms and become bispecific. The Fc structure remains essentially unchanged apart from potential changes due to differences in glycosylation or allotype. Fab arm exchange is proposed to be stochastic and dynamic.

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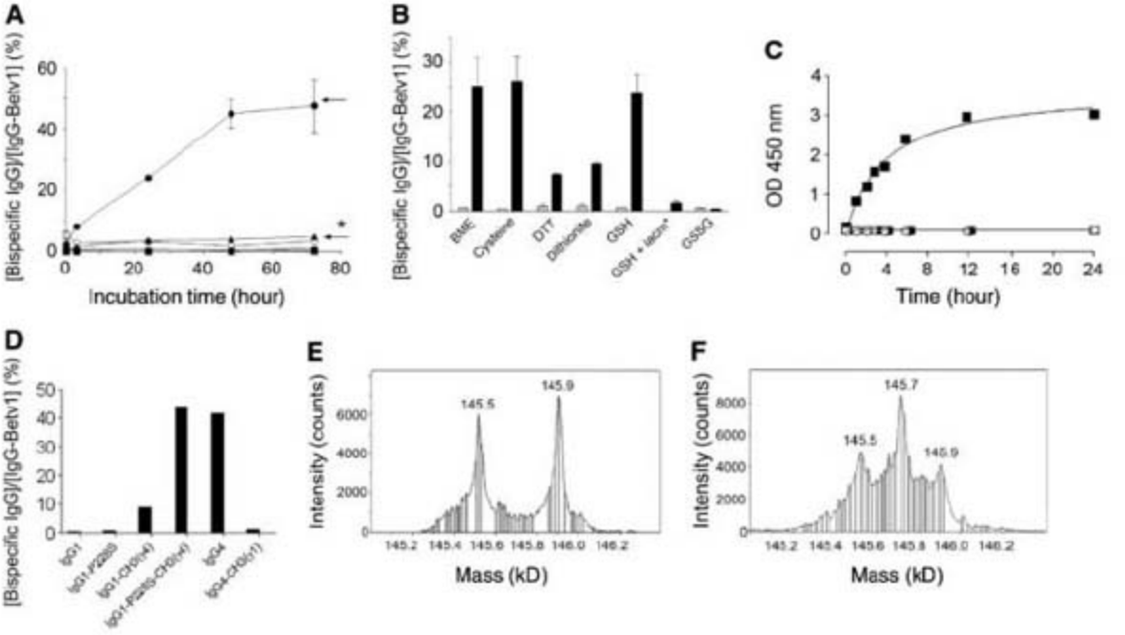

Fig. 2. Induction of IgG4 Fab arm exchange in vitro. **(A)** Incubation of IgG4-Betv1/IgG4-Feld1 mixtures (circles) with human erythrocytes (closed symbols) at 37°C resulted in generation of bispecific antibodies; no bispecificity was generated in IgG1 mixtures (squares). As controls, an excess of irrelevant IgG4 was added (triangles) or antibody mixtures were incubated without erythrocytes (open symbols). Error bars represent range of duplicate measurements. **(B)** IgG4-Betv1/IgG4-Feld1 mixtures (black bars) were incubated for 24 hours at 37°C in the presence of different reducing agents, and the generation of bispecific IgG was determined. IgG1 antibody mixtures were used as controls (gray bars). Error bars represent SEM calculated from three measurements. **(C)** IgG4-CD20/IgG4-EGFr mixtures (squares) were incubated at 37°C with (closed symbols) or without (open symbols) 0.5 mM GSH. The formation of bispecific antibodies was measured in ELISA. OD_{450}, optical density (absorbance) at 450 nm. Mixtures of IgG1 antibodies were used as controls (circles). Data are representative of three experiments. **(D)** IgG1 and IgG4 mutants were prepared for the Betv1 and Feld1 antibodies. P228S represents a point mutation that introduces the IgG4 core hinge sequence into IgG1. $C_H3(\gamma1)$ and $C_H3(\gamma4)$ represent domain swap mutations in which the original third constant domain is replaced with the IgG1 or IgG4 domain, respectively. Fab arm exchange between corresponding mutants is shown. **(E)** IgG4-EGFR/IgG4-CD20 mixtures were incubated for 24 hours in the absence (E) or presence (F) of 0.5 mM GSH, after which the antibodies were deglycosylated with peptide *N*-glycosidase F, and the molecular masses of the resulting antibodies were determined by ESI-TOF mass spectrometry. Deconvoluted ESI-TOF spectra are shown. Data are representative of two experiments.

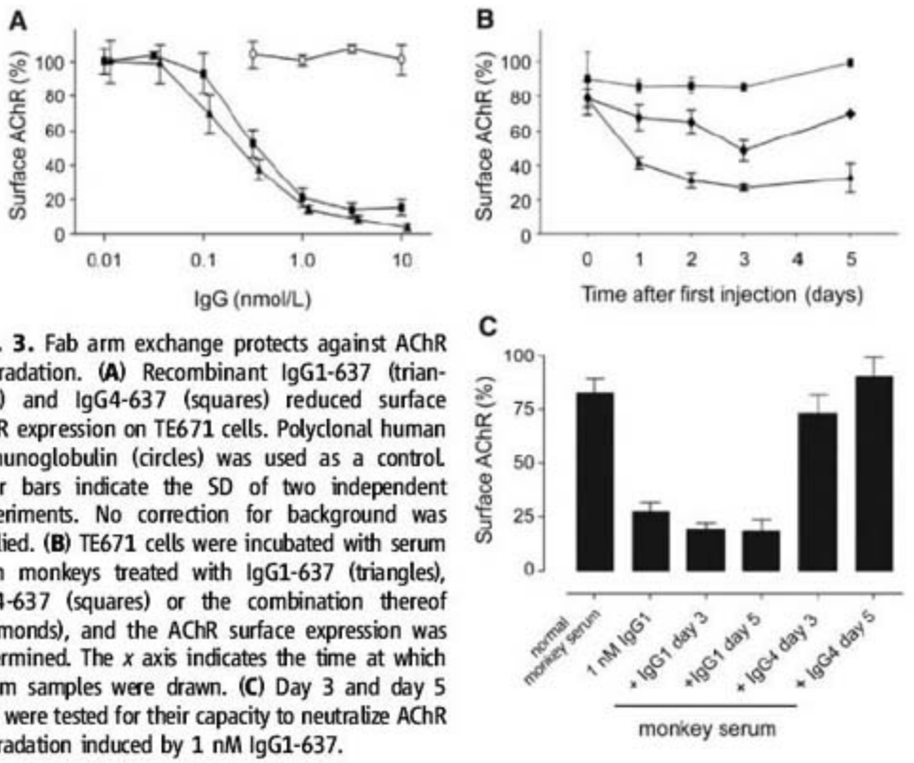

Fig. 3. Fab arm exchange protects against AChR degradation. **(A)** Recombinant IgG1-637 (triangles) and IgG4-637 (squares) reduced surface AChR expression on TE671 cells. Polyclonal human immunoglobulin (circles) was used as a control. Error bars indicate the SD of two independent experiments. No correction for background was applied. **(B)** TE671 cells were incubated with serum from monkeys treated with IgG1-637 (triangles), IgG4-637 (squares) or the combination thereof (diamonds), and the AChR surface expression was determined. The *x* axis indicates the time at which serum samples were drawn. **(C)** Day 3 and day 5 sera were tested for their capacity to neutralize AChR degradation induced by 1 nM IgG1-637.

Table 1. IgG4-637 protects monkeys from IgG1-637–induced myasthenia gravis. Total cumulative dose is the sum of antibodies injected as three doses on three consecutive days. Clinical symptoms started between day 1 and 5 post injection and lasted up to 7 days. At the peak of the disease, animals were hypoactive; could not climb because of weakness of the limbs, hands, and feet; and had difficulty eating.

Antibody	Total cumulative dose (mg/kg)	Animals (*n*)	Clinical symptoms
IgG1-637	1.5	1	No (0/1)
IgG1-637	3	1	No (0/1)
IgG1-637	15	1	Yes (1/1)
IgG1-637	5	4	Yes (4/4)
IgG4-637	15	2	No (2/2)
IgG1-637 + IgG4-637	5 + 15	5	No (5/5)

body represented 50% of the total antibody mass in the mixture, which indicated a stochastic exchange (Fig. 1B).

We investigated how Fab arm exchange contributes to the anti-inflammatory properties of IgG4 in an animal model in which antibody-mediated cross-linking plays an important role in disease pathogenesis. Experimental autoimmune myasthenia gravis (MG), in which autoantibodies against acetylcholine receptor (AChR) induce muscle weakness, represents such a model (*19*). The human AChR-specific antibody IgG1-637 is a patient-derived antibody (*20*) that induces AChR degradation as can be monitored in vitro using rhabdomyosarcoma TE671 cells. Both IgG1-637 and IgG4-637 antibodies reduced TE671 cell surface AChR levels to the same extent (Fig. 3A), which indicated that these antibodies reacted similarly in vitro. IgG1-637 is a pathogenic antibody, and it induced MG disease dose-dependently in rhesus monkeys (Table 1). The IgG4-637 antibody, in contrast, was not pathogenic (Table 1). To assess whether IgG4-637 might protect against IgG1-637–induced disease, we injected IgG4-637, followed by challenge with a pathogenic dose of the IgG1 antibody. All animals were protected ($n = 5$), which represents a significant difference compared with treatment with IgG1-637 alone ($P < 0.01$; two-tailed Fisher's exact test) (Table 1). Notably, protection against MG disease correlated with an in vivo decrease of AChR cross-linking activity of the injected IgG4 antibody. Thus, serum

from an IgG1-637–treated monkey induced strong AChR degradation, in contrast to serum from a monkey injected with the IgG4 antibody (Fig. 3B). The latter serum, moreover, prevented AChR degradation by IgG1-637 in an in vitro mixing experiment (Fig. 3C). Finally, serum from an animal treated with both antibodies induced only moderate degradation. The IgG4-637 antibody, which induced AChR degradation before injection (Fig. 3A), apparently acquired non–cross-linking and protective activity in vivo.

Antibody function is regulated by posttranslational modifications. Fucosylation in the Fc domain, for example, affects immune cell activation by modulating affinity for Fc receptors (*21*). Sialylation has been shown to endow IgG with anti-inflammatory activity (*22*), but that cannot explain our findings, as none of the antibodies used contained sialic acid. Dynamic Fab arm exchange therefore represents a novel type of posttranslational modification, which serves as an additional mechanism for generating anti-inflammatory activity. The mechanism by which IgG4 Fab arm exchange occurs in vivo likely requires the reducing environment in blood or at cell surfaces to facilitate the breaking of inter–heavy chain disulfide bonds located in the hinge region. Indeed, the addition of reducing compounds, such as GSH, to purified IgG4 alone was sufficient to induce in vitro Fab arm exchange. GSH, present in all cell types, may well perform this role in vivo, and so additional cofactors, chaperones, or receptors, as hypothesized for PDI and FcRn previously (*10*), may therefore not be essential. An important second antibody heavy chain interface is located between the C_H3 domains, which we show to be critically involved in Fab arm exchange. Elucidating the contribution of specific C_H3-domain amino acid contacts to the mechanism of this reaction requires further investigation.

We show that IgG4 molecules acquire two distinct Fab arms by Fab arm exchange, which, when derived from polyclonal plasma IgG4, are (usually) directed against unrelated antigens. Fab arm exchange, furthermore, is dynamic, and combinations of certain specific Fab arms are therefore only expected to exist transiently. IgG4 molecules thereby lose their ability to cross-link antigen and to form immune complexes under most conditions. IgG4, often induced by chronic antigen stimulation, then may interfere with immune complex formation by other antibody isotypes and may dampen inflammatory reactions. In specific immunotherapy with allergen in allergic rhinitis, for example, increases in allergen-specific IgG4 levels indeed correlate with clinical responses (*7*, *23*). A first proof of concept using monoclonal antibodies indicates that the formation of non–cross-linking IgG4 antibodies in vivo provided protection against a pathogenic antibody in experimental autoimmune MG.

Our results have an impact on immunotherapy with IgG4 monoclonal antibodies. The in vivo instability and dynamics of IgG4 introduce unpredictability, which is undesirable for human immunotherapy. Future studies should address the contribution of IgG4 Fab arm exchange to in vivo activity of therapeutic IgG4 monoclonal antibodies.

In summary, antibodies of the IgG4 isotype are shown to be dynamic molecules, undergoing Fab arm exchange in vivo and in vitro. The ability to engage in Fab arm exchange appears to be an inherent feature of IgG4 that involves the third constant domain in addition to the hinge region and that only requires a reducing environment to be activated. This novel protein modification challenges the commonly accepted one antibody–one antigen paradigm and redefines our thinking about the role of IgG4 in antibody-mediated immunity and the application of IgG4 monoclonal antibodies to immunotherapy.

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Materials and Methods
Figs. S1 to S6
Table S1
References

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Functional Architecture and Evolution of Transcriptional Elements That Drive Gene Coexpression

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Transcriptional coexpression of interacting gene products is required for complex molecular processes; however, the function and evolution of cis-regulatory elements that orchestrate coexpression remain largely unexplored. We mutagenized 19 regulatory elements that drive coexpression of *Ciona* muscle genes and obtained quantitative estimates of the cis-regulatory activity of the 77 motifs that comprise these elements. We found that individual motif activity ranges broadly within and among elements, and among different instantiations of the same motif type. The activity of orthologous motifs is strongly constrained, although motif arrangement, type, and activity vary greatly among the elements of different co-regulated genes. Thus, the syntactical rules governing this regulatory function are flexible but become highly constrained evolutionarily once they are established in a particular element.

Gene products that are involved in the same molecular process must be coordinately expressed. Transcriptional coexpression is achieved by regulatory proteins and their target cis-regulatory elements that promote gene transcription in overlapping spatiotemporal distributions (*1*–*7*). The function of a cis-element is encoded in its molecular architecture: a nucle-

otide sequence with instantiations (motifs) of the binding sites (motif types) for one or more transcription factors arranged with functionally significant motif combinations, orientations, or spacing. We address the molecular architecture of cis-elements driving gene coexpression and how the sequence and function of such elements evolves.

Because motifs are the functional units within a cis-element, analysis of a cis-element's molecular architecture and evolution requires an experimental system that allows quantification of each motif's activity, in a sufficiently large number of coexpressed genes whose functions have been maintained throughout evolution. The urochordate *Ciona* harbors such a system in the form of 19 genes that are coexpressed in the 36 muscle cells of the developing embryo (*6*). Of these 19 genes, 17 function in the same macromolecular complex, underscoring the requirement for tight coexpression. The genes include six single-copy loci from *C. savignyi* and their six orthologs in the sister species, *C. intestinalis*: α-tropomyosin 1 (AT1), α-tropomyosin 2 (AT2), myosin binding protein (MBP), troponin I (TI), troponin T (TT), and creatine kinase (CK). The remaining seven genes comprise two or three paralogs each of the multicopy gene families muscle actin (MA), myosin light chain (MLC), and myosin regulatory light chain (MRLC) from *C. savignyi* (fig. S1). The three motifs that mediate muscle-specific transcription in *Ciona* in general, and of these loci in particular, are the cyclic adenosine 5′-monophosphate response element (CRE) (*6*, *8*), the MyoD motif (*9*–*11*), and the Tbx6 motif (*12*) (fig. S2).

We investigated the functional architecture of the 19 cis-elements by a comprehensive mutagenesis effort coupled with a whole-embryo expression assay (*13*–*15*). Each reporter construct harboring specifically mutagenized sequences was transfected into hundreds of developing embryos. Activity of a mutagenized element was measured as the percentage of muscle cells expressing the reporter, which we show to correlate with average transcript levels [fig. S4 and supporting online material (SOM) text, section 3]. A first few hundred constructs, assayed in over 2000 transfections, defined the cis-elements responsible for the majority of function of each locus (Fig. 1 and table S1). We then dissected each cis-element using 220 constructs with small deletions [5 to 10 base pairs (bp)] or site-directed mutants that removed putative motifs in isolation or different combinations. Our quantitative results are based on 1237 transfections (five biological replicates per construct), which yielded a total of 85,506 transgenic embryos (table S2).

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A quantitative and biologically meaningful representation of the functional architecture of each cis-element required an analysis framework to estimate the activity of each motif. To choose a framework, we needed to assess the relative importance of genetic interactions between motifs. Using the subset of the data that was appropriate for interaction analyses, we determined that most of the cis-elements examined functioned with little epistasis (SOM text, section 4, and fig. S5). Further evidence for motif independence was obtained by motif substitution experiments (SOM text, section 5, and fig. S6). This indicated that we could use multivariate regression (*16*) as the analytical framework to quantify motif activity.

Model predictions approximate the observed data well and are robust to several analytical scenarios (SOM text, section 6, fig. S7, and tables S1 and S3). After considering the advantages and drawbacks of these scenarios, we chose to continue our analyses with additive regression models (SOM text, section 6). These models explain 30 to 89% (mean 67%) of the variance of expression at each element (table S1), again underscoring that genetic independence explains most of the data well. Consistent with additivity, we express motif function in "expression frequency units" (efu), meaning that a motif with an inferred activity of x efu increases by x the percentage of muscle cells in which expression is detected (SOM text, section 3). The mean per-element fraction of activity attributed to the motifs is 83%. The 77 motifs affect element activity by –0.14 to 0.45 efu (Fig. 2A), with 39 motifs having significantly nonzero activating function (partial regression coefficient t statistic, $P < 0.05$).

Having obtained quantitative estimates of motif activity, we examined each element's functional architecture. Apart from the obvious clustering of functional motifs, we were unable to discern any features (such as spacing, order, and relative orientation of motifs) that might explain the functions of individual motifs or of the elements as a whole, which would have shed light on organizational principles of regulatory elements. Indeed, there is notable heterogeneity among the loci: Elements are built from motifs of widely varying activity, from different combinations of motif types, and in diverse arrangements (Fig. 2B). For example, the cis-element at CK spans 31 bp and consists of one intermediate and one strong Tbx6 motif, whereas the AT1 cis-element consists of two weak CRE motifs, followed by two intermediate Tbx6 motifs and

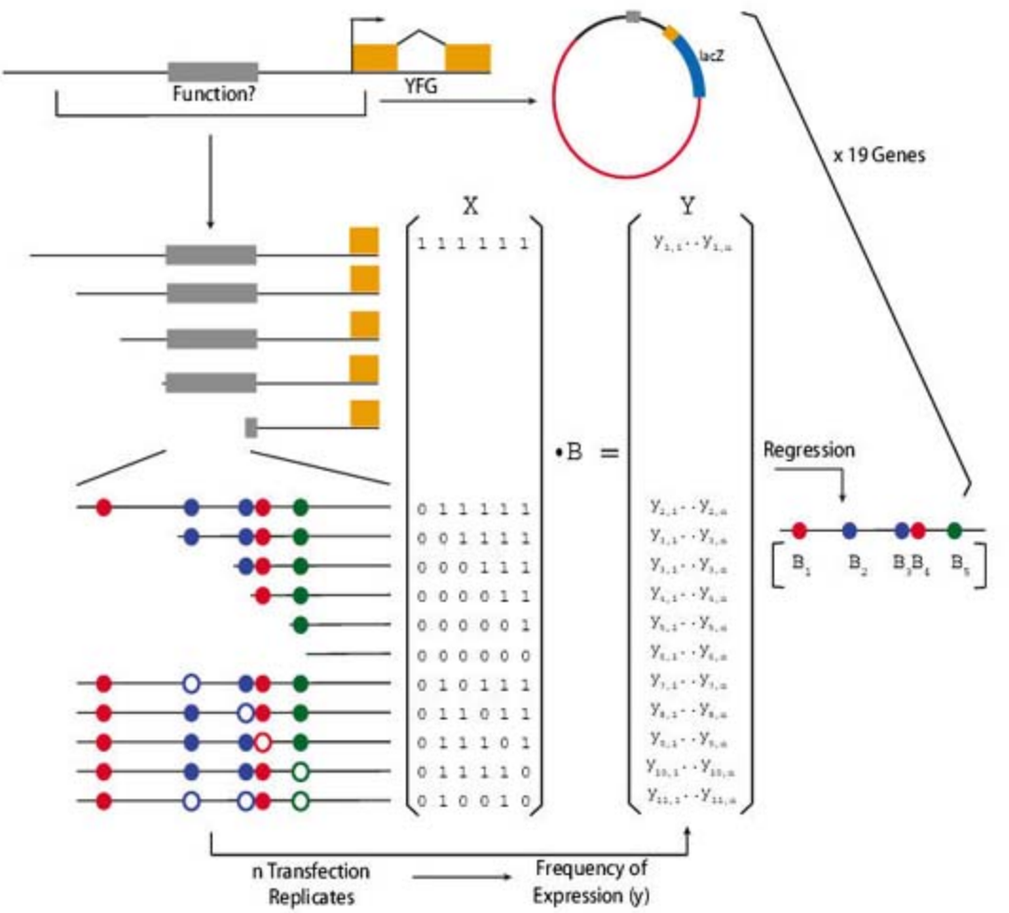

Fig. 1. Experimental design. For each of 19 loci, initial deletion series (truncated lines) locate regions of concentrated function (gray bar). Fine-scale deletions and site-directed mutations (open circles) target putative motifs (solid circles). Set of constructs is represented as matrix X of categorical explanatory variables (ones and zeroes) whose replicated transfections yield expression measurements (matrix Y of $y_{n,i}$). Functional contributions of individual motifs (B_1 to B_5) are estimated with regression models. YFG, your favorite gene.

a strong MyoD motif, across 35 bp. Although motif independence is prevalent, elements do somewhat differ in how much genetic interaction exists. At MBP and AT2, for example, the additive model explains the data very well with high correlations between the predictions and the actual data ($r^2_{Cs\text{-}MBP}$ = 0.83, $r^2_{Cs\text{-}AT2}$ = 0.77; tables S1 and S3) and with little function unexplained by the model. Function at MA1, by contrast, is not described as well by models without interactions (table S3).

Conceivably, the heterogeneous regulatory architectures specify subtle differences in expression pattern or timing during developmental stages or physiological conditions not assayed here. It is clear, however, that the genes' tight coexpression in the embryonic tail muscle is achieved by a common and restricted set of three transcription factors acting upon vastly different cis-element architectures, the diversity of which defies the expectation that commonalities in design underlie co-regulation.

In stark contrast to the apparent flexibility of regulatory architecture, we observed little change in motif activity, order, or composition between orthologous elements of *C. intestinalis* and *C. savignyi*. (Neutral sequence divergence between the two *Ciona* species is approximately equivalent to that between mammals and birds, ruling out the possibility that these sequences have not been afforded enough time to accumulate change.) At single-copy genes, 26 of the 27 motifs with statistically significant activity have a clearly orthologous counterpart. Orthologous motifs drive very similar, in many cases indistinguishable, amounts of activity (Fig. 3A). For example, both MBP orthologs are regulated by a strong MyoD, a weak Tbx6, and a weak CRE motif, with less than 0.039 efu average deviation in individual motif activity. In total, the activity of orthologous regulatory motif pairs is highly correlated between the two species (Spearman's $\rho = 0.61$, $P < 0.005$; Fig. 3B). Thus, co-regulated gene expression at these loci has been maintained by conserving the locus-specific ancestral cis-regulatory architectures, with purifying selection tolerating little functional flexibility.

Strong constraint is evident at the sequence level as well. Functional regulatory motifs exhibit far fewer substitutions than the genome-wide average ($P < 3.8 \times 10^{-10}$) (SOM text, section 7, and fig. S8A). The pairwise identity between orthologous functional motifs is 79%, whereas the genome-wide background identity is <20% (including insertions and deletions). Sequence identity markedly drops off outside the boundaries of the functional motifs (Spearman's $\rho = -0.57$, $P < 0.05$), reaching genome-wide background levels within 12 bp (fig. S8B). Finally, there is less population genetic variation in the motifs than on average in the genome (*17*) (SOM text, section 7, and fig. S10). This demonstrates that the motif sequences are subject to far greater evolutionary constraint than flanking sequence and that the functional motifs themselves are the units maintained by purifying selection.

The sequence changes that have occurred are not distributed evenly among the orthologous motifs, with functionally strong motifs having accumulated fewer substitutions than weak motifs. Notably, motif activity is significantly correlated with percent identity (Spearman's $\rho = 0.35$, $P < 0.05$). This is likely due to strong regulatory motifs being responsible for a larger fraction of the total function of a regulatory element; substitutions in them will therefore result in greater phenotypic consequences and be subject to stronger levels of purifying selection, decreasing the evolutionary rate of the element.

Further emphasizing that the activity of an element is controlled tightly by evolutionary pressures is a case of compensatory evolution in AT2. Two Tbx6 motifs (Fig. 3, A and C) are functionally strong in one species and weak in the other, in a complementary pattern. These activity differences correlate with substitutions away from or toward the motif consensus (Fig. 3C). The functional differentiation of these cis-regulatory motifs did not result from motif gain or loss but from base substitutions that modified motif activity.

Comparison of the cis-regulatory architectures of the three groups of paralogs from *C. savignyi* presents a strong contrast to the highly constrained orthologous cis-elements. The paralogous architectures show a high degree of differentiation in the form of element and motif-level sequence turnover as well as functional divergence of well-aligned motifs (Figs. 2B and 3D). Thus, whereas purifying selection acting on orthologous motifs in single-copy genes is strong enough to maintain conservation of regulatory motif sequence and function over long evolutionary distances, the paralogous motifs of clusters of genes that encode the same protein exhibit far greater rates of turnover. We speculate that this greater flexibility in elements of clustered multicopy genes is tolerated because changes in

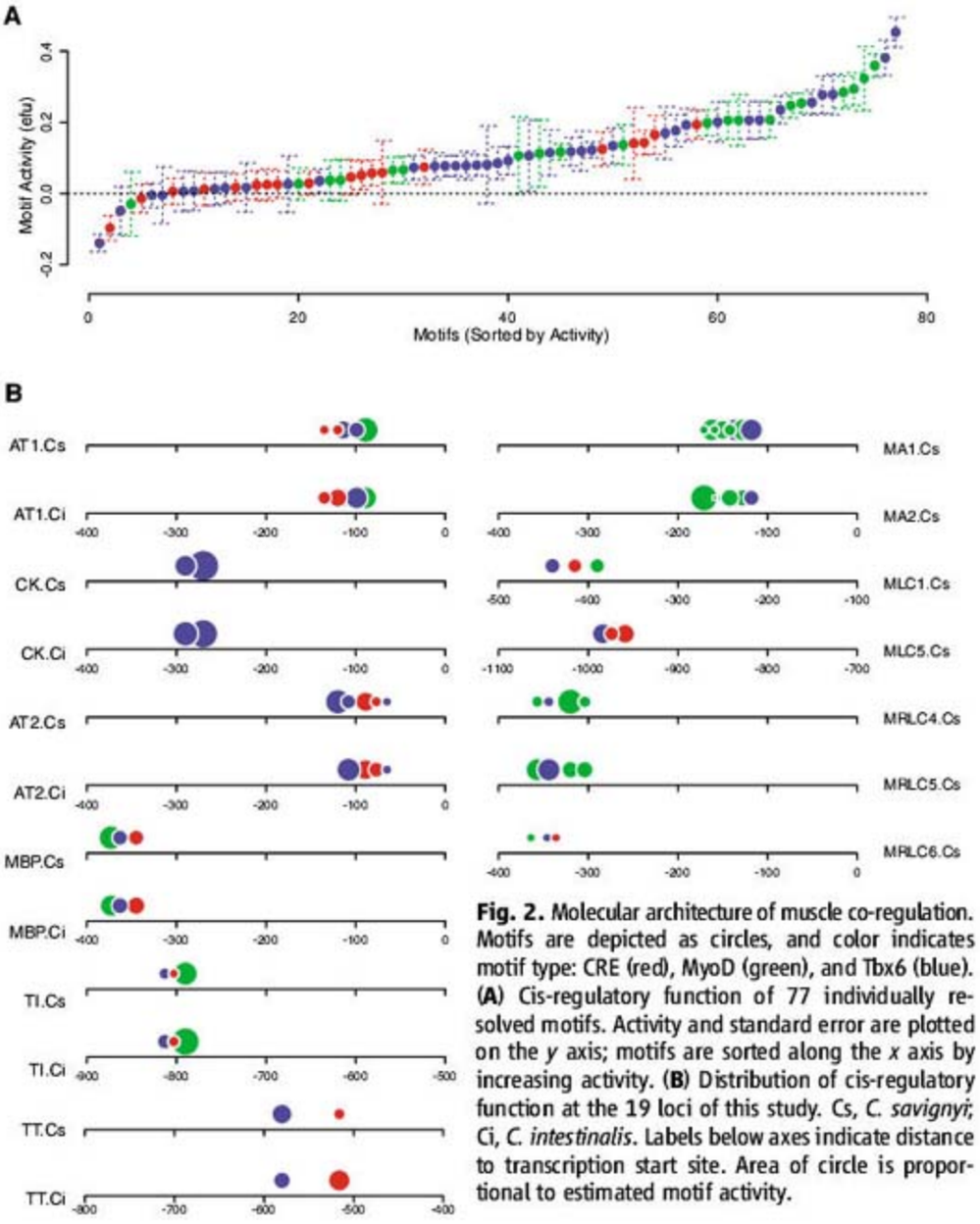

Fig. 2. Molecular architecture of muscle co-regulation. Motifs are depicted as circles, and color indicates motif type: CRE (red), MyoD (green), and Tbx6 (blue). **(A)** Cis-regulatory function of 77 individually resolved motifs. Activity and standard error are plotted on the *y* axis; motifs are sorted along the *x* axis by increasing activity. **(B)** Distribution of cis-regulatory function at the 19 loci of this study. Cs, *C. savignyi*; Ci, *C. intestinalis*. Labels below axes indicate distance to transcription start site. Area of circle is proportional to estimated motif activity.

the activity of one element have a small effect on the total function of the cluster.

The two most prominent developmental mechanisms that build a multicellular organism are pattern formation and cellular differentiation. Previous studies of regulatory architecture and evolution were conducted in pattern formation systems, either by leveraging sequence comparisons and broad functional genomic data (*18*–*20*) or by studying a single regulatory element in detail (*21*–*24*). By contrast, we dissected the regulation of coexpression during cellular differentiation and introduced a quantitative framework for targeted experimental analysis of motif function. Using the *Ciona* muscle system, we demonstrated that coexpression is driven by regulatory motifs of broadly varying activity assembled into a diverse array of cis-elements. Despite this flexibility in cis-regulatory architecture, motif-level sequence and function are exquisitely maintained in distantly related orthologs. Thus, whereas a diversity of cis-regulatory architectures can generate nearly identical phenotypic outputs, the fitness landscapes separating them appear to be sufficiently rugged to constrain their evolution (*25*).

Our findings have implications for understanding genetic variation in such co-regulatory systems. Polymorphisms in cis-elements will range in phenotype, depending on the amount of activity that the affected motif contributes to the function of its element; the most direct evidence for this view is the wide range of effects on cis-element function by the individual motif mutants we tested. Similarly, a polymorphism in a trans-acting factor will not affect expression of all targets equally but will instead have a target-specific effect whose magnitude is determined by the architecture of the target's cis-element. These conclusions highlight the challenges that lie ahead for interpretation of genetic variation in gene regulatory systems, including those of vertebrates, *Ciona*'s most advanced close relatives.

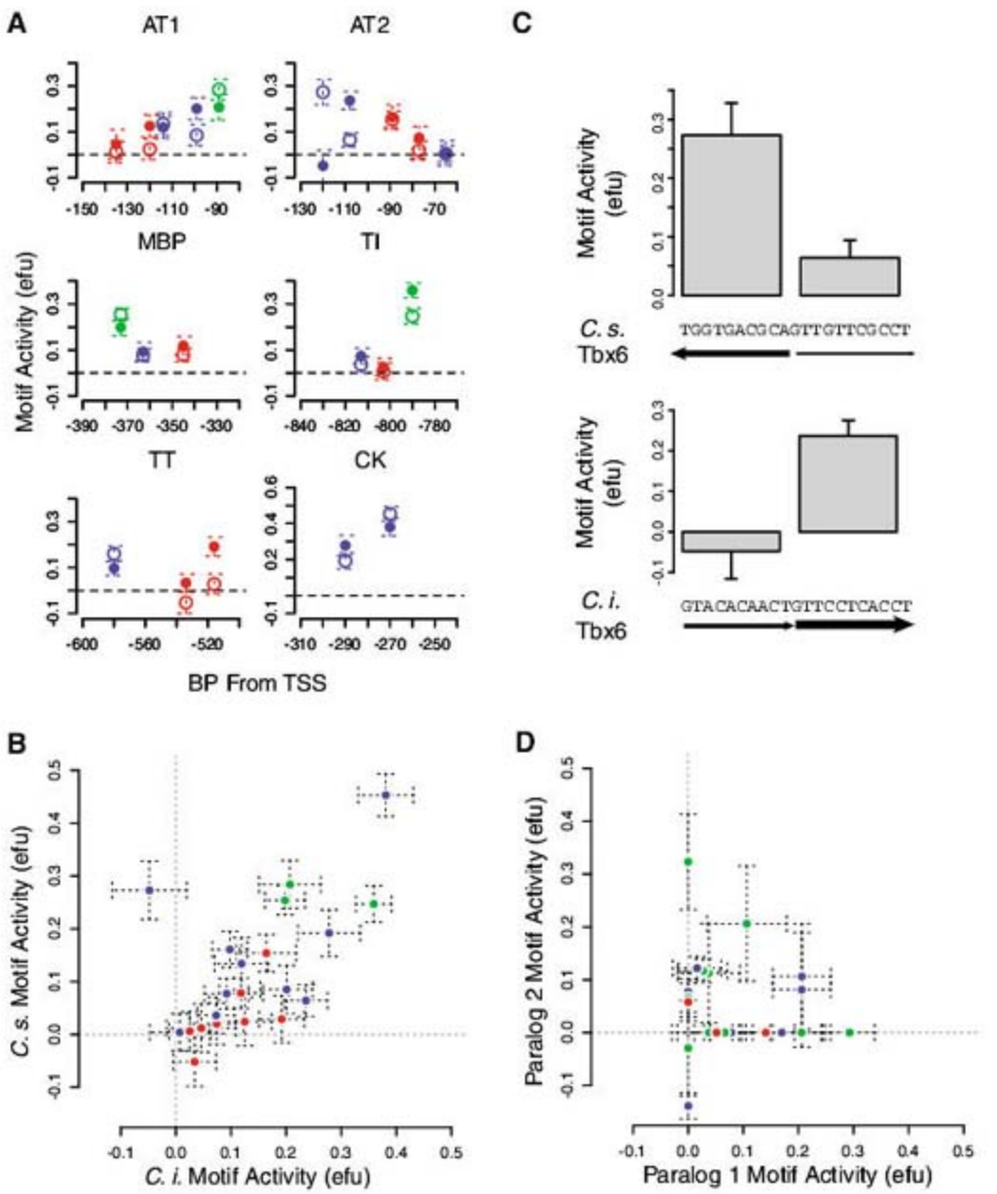

Fig. 3. Evolution of motif activity. **(A)** Motif-level distribution of regulatory activity at six orthologous gene pairs. Distance from transcription start site and motif activity are plotted along the *x* and *y* axes, respectively. Open and solid circles represent individually resolved *C. savignyi* and *C. intestinalis* motifs, respectively. Colors are same as in Fig. 2. **(B)** Conservation of orthologous motif activity. *C. intestinalis* and *C. savignyi* motif activity plotted against each other. **(C)** Compensatory evolution of AT2 regulatory elements for *C. savignyi* (top) and *C. intestinalis* (bottom). Arrow direction and thickness represent Tbx6 motif orientation and strength of match to its position-specific scoring matrix. Bar plots depict activity of each Tbx6 motif, as estimated from additive regression models. **(D)** Functional turnover in paralogous motifs. Plotted as in (B). Error bars in all panels depict standard error.

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Supporting Online Material

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Materials and Methods
SOM Text
Figs. S1 to S11
Tables S1 to S3
Marker (Java image annotation tool)
References

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Mutual Feedbacks Maintain Both Genetic and Species Diversity in a Plant Community

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The forces that maintain genetic diversity among individuals and diversity among species are usually studied separately. Nevertheless, diversity at one of these levels may depend on the diversity at the other. We have combined observations of natural populations, quantitative genetics, and field experiments to show that genetic variation in the concentration of an allelopathic secondary compound in *Brassica nigra* is necessary for the coexistence of *B. nigra* and its competitor species. In addition, the diversity of competing species was required for the maintenance of genetic variation in the trait within *B. nigra*. Thus, conservation of species diversity may also necessitate maintenance of the processes that sustain the genetic diversity of each individual species.

A wealth of theoretical and empirical research has sought the mechanisms that enable multiple competing species to coexist in a given area (*1*–*3*). Similarly, much research in population and quantitative genetics explores processes that promote the maintenance of allelic variation (i.e., genetic diversity) at loci, especially for traits with potential selective impacts (*4*–*6*). Recent theoretical and empirical studies suggest that diversity at one level may depend on the diversity of the other (*7*–*11*). Selection pressure on specific traits varies with community composition, suggesting a role for species diversity in maintaining genetic diversity (*12*). Additionally, genetic diversity in plant populations can determine the species diversity of associated arthropods and microbes (*7*–*9*). However, no studies have explicitly studied how species and genetic diversity may interact, creating feedback loops that simultaneously maintain diversity at each level.

Plants in the family Brassicaceae all produce glucosinolates (amino acid–derived secondary compounds that consist of a β-thioglucose residue, an *N*-hydroxyiminosulfate moiety, and a variable side chain) that, in the presence of the myrosinase enzyme, break down into isothiocyanates and other products toxic to many herbivores, bacteria, mycorrhizal fungi, and other plants (*13*–*15*). Thus, glucosinolates affect a host of organisms and are ecologically important compounds in natural communities. We tested the hypothesis that changes in the mean level of a glucosinolate allelochemical could lead to changes in plant community structure (potentially through allelopathic or antimycorrhizal effects) that, in turn, would feed back to affect selection on the allelochemical. *Brassica nigra* was selected for study because *B. nigra*, unlike most other members of the Brassicaceae, has the desirable property that 90 to 99% of its glucosinolates are in the form of a single compound: sinigrin (allylglucosinolate), which is a heritable trait (*16*, *17*). Because of sinigrin's effects on heterospecific plants and mycorrhizal fungi (mutualists that benefit most plant species but not members of the Brassicaceae), we hypothesized that investment to sinigrin should benefit *B. nigra* genotypes competing with heterospecifics but not conspecifics.

To determine whether there were possible feedbacks between natural variation in community composition and variation in *B. nigra* sinigrin concentration, we sampled naturally occurring *B. nigra* individuals along a gradient ranging from a monospecific stand of pure *B. nigra* to areas dominated by a mix of other species (heterospecifics), with only a few widely spaced *B. nigra* individuals. We estimated the percentage of cover of four functional groups (*B. nigra*, heterospecific forbs, grasses, and bare ground) in a 1-m-diameter circle around each selected individual. We also measured the sinigrin concentration in leaves and final fitness for each individual (*18*).

We found that the selective value of sinigrin increased as the community became dominated by heterospecifics (Fig. 1). However, for *B. nigra* individuals growing mostly with conspecifics, high sinigrin concentrations were correlated with lower fitness (Fig. 1), resulting in a significant interaction between the effects of sinigrin concentration and percentage of cover of *B. nigra* on the fitness of individual plants ($F_{1,43} = 6.065$, $P < 0.05$, $R^2 = 0.278$, multiple linear regression). Additionally, the cover of heterospecific forbs immediately surrounding the sampled *B. nigra* individuals declined significantly with increasing sinigrin concentrations in the sampled *B. nigra* plants (Fig. 2). Thus, not only does the selective value of sinigrin concentration seem to depend on community composition, but the community composition may also depend on the sinigrin concentrations of individual plants.

Our observations suggest that cyclic dynamics between selection pressures and community composition could lead to the simultaneous maintenance of both genetic diversity in sinigrin genes and species diversity in the plant community. To test this hypothesis rigorously, we performed a community invasibility experiment. Using plants from six naturally occurring populations and three generations of artificial selection, we created lines of high- and low-sinigrin *B. nigra*; the mean values of sinigrin in both lines were within the natural range found in these populations (*18*).

For community diversity, we collected seeds from three abundant, co-occurring, and phylogenetically diverse competitor species [*Amsinckia menziesii* (Boraginaceae), *Sonchus oleraceus*

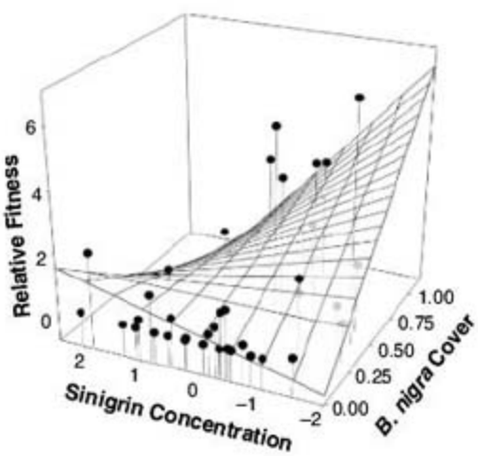

Fig. 1. Fitness of naturally occurring *B. nigra* individuals versus their sinigrin concentration (standardized) and the percentage of cover of *B. nigra* in a 1 m^2 circle around the target plant (arcsine transformed). Black dots represent actual data points, and the mesh surface graphs the predicted values from a multiple regression, including the two terms and their interaction (*18*). Lines running left to right on the surface can be interpreted as predicted selection gradients at different levels of *B. nigra* cover.

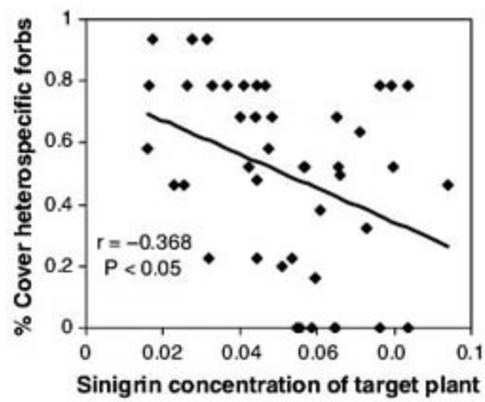

Fig. 2. Percentage of cover of heterospecific forbs in a 1 m^2 diameter circle surrounding the sampled *B. nigra* individuals versus the sinigrin concentration of those sampled individuals. The heterospecific forbs consisted of a mix of species including *A. menzeseii*, *S. oleraceus*, *M. parviflora*, and *Silybum marianum*.

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(Asteraceae), and *Malva parviflora* (Malvaceae)]. *B. nigra* grows naturally both in dense monospecific stands and in diverse heterospecific stands with these three species in the field (Fig. 2). We made three replicated community types in the field: high-sinigrin *B. nigra* monocultures, low-sinigrin *B. nigra* monocultures, and a three-species mixed heterospecific community. Each community consisted of 24 neighbor plants surrounding one target invader. Into each synthetic community, we introduced one focal plant (as an "invader"). Invader plants were either a high- or low-sinigrin *B. nigra* or a heterospecific individual from one of the three other species. Plants were grown 25 cm apart, with 3-m alleys between communities. For each community type, we grew 11 communities with a high-sinigrin invader, 11 with a low-sinigrin invader, and 7 with each heterospecific species as the invader (*18*). Thus, sinigrin concentrations and community composition (hetero- or conspecific) vary among our experimental communities, resulting in genetic and species diversity at the field rather than the plot scale. Theory has shown that competitive coexistence of species or alleles occurs only when all species (or genotypes) can invade when rare (*19*). Thus, this design allows us to test directly whether the genetic variation in sinigrin among our experimental communities will lead to the maintenance of species diversity (and vice versa) by testing whether all species and genotypes can invade at least one community type other than their own.

Consistent with observational data in the field, we found that high-sinigrin *B. nigra* invaders had greater fitness than low-sinigrin *B. nigra* genotypes when invading diverse heterospecific communities. In contrast, low-sinigrin genotypes were better than high-sinigrin genotypes at invading monospecific stands of *B. nigra*, regardless of the sinigrin level of the *B. nigra* community [invader genotype (high versus low sinigrin) by community (*Brassica* versus heterospecific) interaction; log-likelihood ratio (LR) = 4.10, $P < 0.05$] (Fig. 3, generalized linear model). Thus, the fitness of a *B. nigra* genotype depends on the community composition (diverse versus monoculture) that it invades.

Heterospecific invaders were sensitive to the genotype of *B. nigra* and had significantly lower fitness in communities of high-sinigrin versus low-sinigrin *B. nigra* genotypes [community (high versus low), LR = 6.54, P = 0.01] (Fig. 3). Despite low sample sizes, two of the three heterospecific species (*A. menziesii* and *S. oleraceus*) showed significant reductions when analyzed alone (LR = 4.05, $P < 0.05$ and LR = 5.41, $P < 0.05$ respectively), whereas the third (*M. parviflora*) showed a nonsignificant trend in the same direction.

Coexistence generally requires that species compete more strongly intra- versus interspecifically (*1–3*). Therefore, we also measured the fitness of these three competitor species when invading monospecific communities of their own species, to provide an estimate of pure intraspecific competition for each species. Interestingly, there was no difference in heterospecific invader fitness when invading a monoculture of their own species versus when invading an "average" *B. nigra* monoculture (combining high- and low-sinigrin communities) for any of the three heterospecific species (LR < 0.65, $P > 0.40$ for all). This result suggests that genetic variation among *B. nigra* competitors was more important than differences between competitor species in determining fitness of heterospecific competitors. Thus, if one ignores genetic variation in *B. nigra*, the requirement for coexistence does not seem to be met (for all three species, intraspecific competition is equal to or weaker than interspecific competition with "average" *B. nigra*). Only when one considers the role of genetic variation in the competitive ability of different *B. nigra* lines is coexistence predicted.

The observed differences in heterospecific invader fitness in seed production persisted into the next generation in the field, resulting in higher seedling densities in low-sinigrin communities compared with high-sinigrin communities (all species combined, LR = 5.06, $P < 0.05$; *A. menziesii*, LR = 4.59, $P < 0.05$; *S. oleraceus*, LR = 4.24, $P < 0.05$; *M. parviflora*, LR = 0.433, $P = 0.51$) (Fig. 4). Thus, genetic variation in *B. nigra* affected the population dynamics of competing species.

Because our analyses are based on the comparison of our artificially selected lines, it is possible that any effects we detect are due to pleiotropic effects or genes closely linked to those controlling sinigrin concentrations, rather than the direct action of sinigrin. The evolutionary implications are the same in either case, because our invasion analysis still predicts how sinigrin concentrations are expected to increase or decrease through time, whether through the direct actions of sinigrin or as correlated responses to selection on closely linked genes. Nevertheless, we have some evidence that sinigrin itself may be driving these patterns. Glucosinolates have been extensively studied as defenses against herbivores (*11*, *12*); however, rates of herbivory by generalist and specialist herbivores were generally low and did not differ between community or invader types.

Another possibility is that mycorrhizal fungal communities are altered by sinigrin or its breakdown products. Glucosinolates have known antifungal properties (*13*) and have been proposed to mediate competition between mustards and other plants through their effects on arbuscular mycorrhizal fungal mutualists of competitors (*20*). To explore this possibility, we estimated the mycorrhizal infection potential (MIP) of soils taken from 10 plots of each community type (high- and low-sinigrin *B. nigra* monocultures and mixed communities of the three heterospecifics), using *Sorghum bicolor* as an indicator species (*18*, *21*). The plant community type had a large, significant effect on the MIP of the soil samples ($R^2 = 0.677$, $F_{2,27} = 15.717$, $P < 0.001$, analysis of variance). Soils from under high-sinigrin *B. nigra* communities had significantly reduced MIP compared with soils from low-sinigrin communities, with soils from diverse heterospecific communities intermediate between them (Fig. 5).

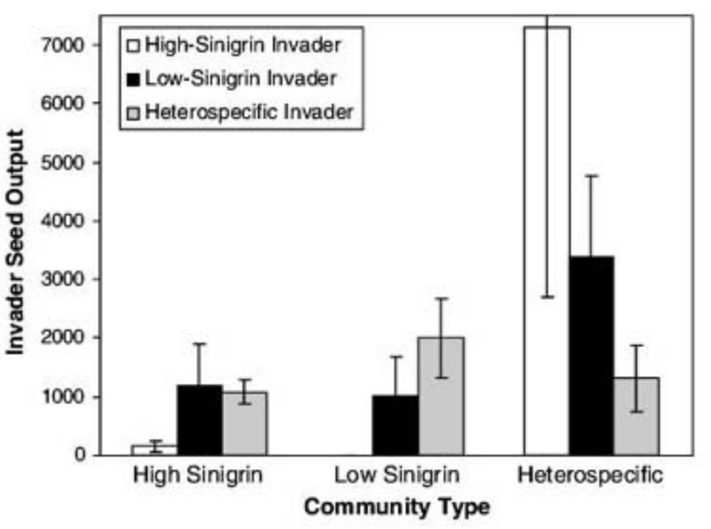

Fig. 3. Fitness of invaders in the three community types (means ± SE). Gray bars represent the average response of the three heterospecific species. See text for statistical comparisons.

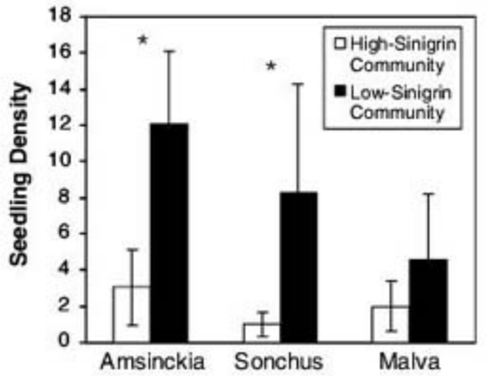

Fig. 4. Seedling density of the three heterospecifics in the following growing season, comparing high- and low-sinigrin *B. nigra* communities into which a heterospecific "invader" of the same species had been planted in the previous year (means ± SE). Asterisks indicate significant ($P < 0.05$) differences between high- and low-sinigrin communities within an invading species.

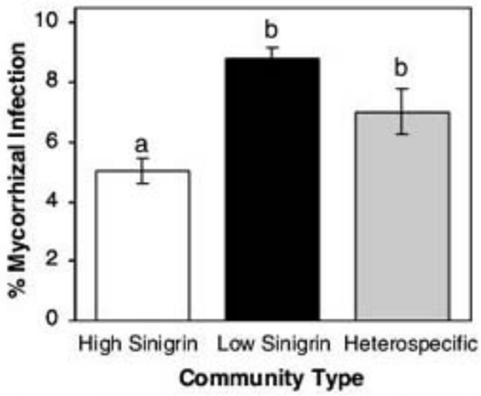

Fig. 5. Mycorrhizal infection potential (measured as the percentage of root sections colonized with mycorrhizal fungus) in soil from high- and low-sinigrin *B. nigra* communities and mixed heterospecific communities (means ± SE). Bars sharing the same letters are not statistically different.

Plants in the Brassicaceae are characteristically nonmycorrhizal, whereas we observed that the three heterospecific competitors, like almost all other angiosperms, do form mutualistic associations with mycorrhizal fungi. Therefore, the observed pattern in MIP among community types may explain the pattern of lower fitness of heterospecifics in high-sinigrin *B. nigra* communities and higher fitness of high-sinigrin *B. nigra* invaders in heterospecific communities. The higher fitness of low-sinigrin *B. nigra* invaders in *B. nigra* monocultures is consistent with a cost of sinigrin production (*22*) and little benefit of high sinigrin levels when competing with nonmycorrhizal *B. nigra* neighbors. Other mechanisms, such as direct allelopathy, may be acting as well (*23*).

Our field data show an intransitive competitive hierarchy between competing species and genotypes leading to cyclical dynamics; high-sinigrin *B. nigra* can invade diverse communities of other species, low-sinigrin *B. nigra* can invade patches of high-sinigrin *B. nigra*, and other species can invade patches of low-sinigrin *B. nigra*. Thus, each species or genotype is able to invade at least one other community type, promoting coexistence through mutual invasibility (*19*). For instance, a diverse, heterospecific community could be invaded by high-sinigrin genotypes of *B. nigra*. As *B. nigra* rises in abundance, displacing heterospecifics, selection will begin to favor lower-sinigrin concentrations. If sinigrin concentrations fall low enough, heterospecific species may be able to reinvade the community, starting the cycle over. This kind of "rock-paper-scissors" intransitivity has been shown to allow coexistence between species (*24*, *25*) and genotypes within species (*26*, *27*), but few studies have investigated intransitive networks consisting of different species and genotypes within one species (*28*)

The experimental results, combined with natural observations, show that in this system, the maintenance of species diversity is dependent on sufficient genetic variation, because without this variation the system would become dominated by *B. nigra* (if sinigrin levels are uniformly high), or by other species (if sinigrin levels are uniformly low). Simultaneously, the maintenance of genetic variation is dependent on species diversity, because selection is predicted to fix sinigrin levels at their lowest level if other competing species are not present. Our experiments show that a trade-off between intra- and interspecific competitive ability in the genetically variable species led to an intransitive competitive hierarchy among competing species and genotypes, thereby promoting coexistence. These results clearly show the potential for genetic variability and microevolution within species to alter community dynamics and structure. Conservation efforts aimed at maintaining species diversity therefore should not overlook the potential impacts of losses of genetic diversity, which could ultimately lead to losses of interacting species.

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Quantitative Imaging of Nitrogen Fixation by Individual Bacteria Within Animal Cells

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Biological nitrogen fixation, the conversion of atmospheric nitrogen to ammonia for biosynthesis, is exclusively performed by a few bacteria and archaea. Despite the essential importance of biological nitrogen fixation, it has been impossible to quantify the incorporation of nitrogen by individual bacteria or to map the fate of fixed nitrogen in host cells. In this study, with multi-isotope imaging mass spectrometry we directly imaged and measured nitrogen fixation by individual bacteria within eukaryotic host cells and demonstrated that fixed nitrogen is used for host metabolism. This approach introduces a powerful way to study microbes and global nutrient cycles.

Bacteria and archaea responsible for biological nitrogen fixation can be found in free-living form (*1*–*3*) or in symbiosis with algae (*4*, *5*), higher plants (*3*, *5*), and some animals (*6*–*8*). Although these microbes are a critical part of the global nitrogen cycle (*9*), there has previously been no means to evaluate this fixation process at subcellular resolution. This is now possible with multi-isotope imaging mass spectrometry (MIMS) (*10*).

Wood and woody plant materials are abundant in the biosphere (*11*) and are important nutrient sources for a variety of fungi and microorganisms (*12*). Yet few animals are able to feed primarily on wood (*13*). Although rich in carbon, wood typically contains two orders of

magnitude less nitrogen per unit of carbon than does animal tissue (*14*). Animals using wood as food must therefore obtain other sources of combined nitrogen for biosynthesis. For example, wood-eating termites are thought to supplement their diet with nitrogenous compounds produced by nitrogen-fixing bacteria inhabiting their gut (*6*). This conclusion is supported by observations that a variety of nitrogen-fixing bacteria have been cultivated from termite guts (*11*) or detected by culture-independent methods (*15*, *16*), and that substantial rates of nitrogen fixation have been measured in association with termite guts and intact termite colonies (*6*). Direct measurement of nitrogen fixation by individual bacteria and of nitrogen use by host cells, however, has remained impossible.

Nitrogen fixation has also been detected in intact specimens of wood-eating marine bivalves of the family Teredinidae (commonly known as shipworms) (*17*), but the site of fixation and the identity of the nitrogen-fixing microorganisms have not been previously determined. Although conspicuous communities of nitrogen-fixing bacteria have not been found in the gut of shipworms (*13*), as they have in termites, dense populations of intracellular bacterial symbionts have been observed in cells (bacteriocytes) in a region of shipworm gills known as the gland of Deshayes (*18*). Moreover, a bacterium (*Teredinibacter turnerae*) capable of fixing nitrogen gas (N_2) in pure culture has been isolated from the gills of numerous shipworm species (*19*, *20*), and its presence in the gill symbiont community of the shipworm *Lyrodus pedicellatus* has been confirmed by in situ hybridization and quantitative polymerase chain reaction analysis (*21*–*23*). These observations raise the questions of whether bacterial symbionts within the gills of *L. pedicellatus* can fix nitrogen and whether this fixed nitrogen is supplied to the host.

We localized and measured nitrogen fixation by individual cells of *T. turnerae* in pure culture, by individual bacterial symbionts in the gill of *L. pedicellatus*, and in subcellular domains of bacteria-free host tissue, using MIMS (*10*) to measure the incorporation of nitrogen gas enriched in the rare stable isotope ^{15}N. With MIMS methodology, quantitative mass images (QMIs) were generated (and the isotope values derived) by quantifying light and heavy isotopes of secondary cyanide ions ($^{12}C^{14}N^-$ and $^{12}C^{15}N^-$) produced by bombardment of the tissue with a primary cesium ion beam (*10*). The tissue was visualized by mapping the distribution of the naturally abundant isotope ^{14}N (as represented by $^{12}C^{14}N^-$) to produce a high-resolution image of nitrogen-containing tissue. A second image, simultaneously acquired in parallel, mapped the distribution of the rare isotope ^{15}N (as represented by $^{12}C^{15}N^-$) (*24*). The incorporation of ^{15}N tracer could then be measured by comparing the two quantitative images to determine the increase of $^{15}N/^{14}N$ ratios as compared to the natural abundance ratio (0.00367). We represented the enrichment of ^{15}N in tissue using a color-coded transform [hue saturation intensity (HSI)] of the isotope ratio values (*10*, *25*).

We first established that MIMS could be used to measure nitrogen fixation by individual cells of *T. turnerae* grown in axenic culture in vitro (*24*). When grown in the presence of $^{15}N_2$ tracer (without a combined nitrogen source in the medium), biological nitrogen fixation could be detected as a time-dependent increase in the $^{15}N/^{14}N$ isotope ratio in individual bacteria. In cultured *T. turnerae*, we found that the mean ^{15}N fraction increased by a factor of 7 to 9 over its natural ratio after 30 min, by a factor of 20 to 28 after 8 hours, and by a factor of 68 after 7 days (Fig. 1, A to C). There was no detectable elevation of the $^{15}N/^{14}N$ ratio in cells of *Enterococcus faecalis*, a bacterium lacking the ability to fix nitrogen, when grown for the same estimated number of generations in the presence of the $^{15}N_2$ tracer and analyzed together with *T. turnerae* in a mixed population (Fig. 1, A to C).

We then applied MIMS to measure the incorporation of ^{15}N by symbionts within gill bacteriocytes in vivo by exposing *L. pedicellatus* to ^{15}N-labeled N_2 while in their intact wood burrows (*24*). After 8 days of exposure, there was a dramatic elevation of the $^{15}N/^{14}N$ ratio in localized regions within the gland of Deshayes, demonstrating the incorporation of gaseous $^{15}N_2$ into the molecular makeup of these regions (Figs. 1D and 2, A to I, and supporting online text). The $^{12}C^{14}N$ QMIs (*10*) showed that these regions appeared to contain densely packed bacteria. We measured nitrogen fixation by thousands of

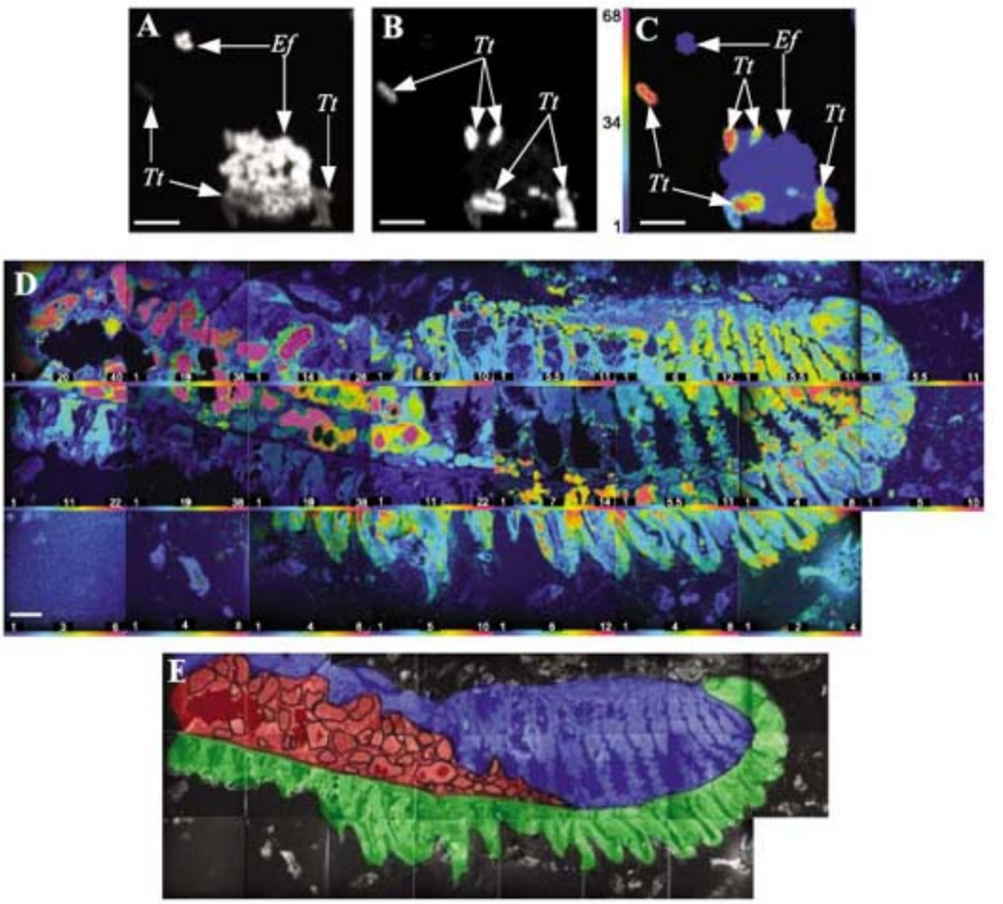

Fig. 1. N fixation by isolated *T. turnerae* bacteria and by bacterial symbionts within the marine bivalve *L. pedicellatus*. (**A** and **B**) Parallel QMIs of one field containing *T. turnerae* (*Tt*) and *E. faecalis* (*Ef*). (A) $^{12}C^{14}N^-$. (B) $^{12}C^{15}N^-$. (**C**) HSI of the ratio (B)/(A). The image is 256 × 256 pixels; acquisition time was 30 min. Scale bar, 5 μm. (**D**) Mosaic of HSI of the $^{12}C^{15}N/^{12}C^{14}N$ ratio from *L. pedicellatus*. Each tile is 100 × 100 μm and 256 × 256 pixels; acquisition time was 120 min per tile. Scale bar, 25 μm. The HSI scales represent the measured $^{15}N/^{14}N$ ratio divided by the natural abundance ratio. The scale ranges from blue (denoting a factor of 1; that is, the natural value) to magenta (denoting an increase over the natural value by at least the factor indicated on the right of each bar). (**E**) Cartoon of (D), outlining the location of the gland of Deshayes (red), interlamellar junctions (blue), ctenidial filaments (green), and bacteriocytes (outlines). In (C), the highest ^{15}N incorporation is seen in *T. turnerae* and none in *E. faecalis*. In (D), the highest ^{15}N incorporation is seen in bacteriocytes of the gland of Deshayes.

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individual symbiotic bacteria. The values of $^{15}N/^{14}N$ ranged from a factor of 17 to a factor of 68 over the natural ratio, with a mean increase of a factor of 39 (Fig. 4A, Table 1, and supporting online text). Furthermore, we were able to successively image the same gill tissue sections, first with transmission electron microscopy (TEM) and then MIMS. The images produced by the two methods could be precisely superimposed, confirming the identity of the densely packed bacteria observed in the MIMS images (Fig. 2, G to I). This enabled us to find that the regions immediately adjacent to the periphery of individual bacteria had a degree of ^{15}N incorporation that was slightly more elevated (but with high statistical significance) than that within the bacteria (supporting online text). These results demonstrate that nitrogen is fixed by endosymbiotic bacteria within the gills of *L. pedicellatus* and suggest that molecules containing fixed nitrogen are transported to the proximity of the bacterial cell surface. The variation in ^{15}N fixation among individual bacteria could reflect differences in the physiological state of symbionts or genetic differences among symbionts within individual bacteriocytes. The latter is consistent with previous observations indicating the coexistence of multiple symbiont ribotypes within individual bacteriocytes in *L. pedicellatus* (*22*). The variation could reflect bacteriocytes at different stages of development (*26*).

The $^{15}N/^{14}N$ ratios were also elevated in gill regions and structures that were free of bacteria, such as in discrete cells located at the base of the gill filaments and in individual cilia in the gill apex where new filaments are formed (Fig. 3, A to C and E to J). We circumscribed hundreds of subcellular regions of interest (ROIs) on these structures and found increased $^{15}N/^{14}N$ values ranging from a factor of 1.4 to a factor of 11 over the natural ratio, with a mean increase of a factor of 5 for ROIs in both the ctenidial (gill) filaments and interlamellar junctions (Fig. 4A, Table 1, and supporting online text). We confirmed the absence of symbionts in these ROIs by TEM analysis (Fig. 3D). Although ^{15}N was incorporated in symbiont-free regions, the highest values in these regions were lower than the minimum value measured in the symbiotic bacteria (Fig. 4A and Table 1). The observed distribution of ^{15}N incorporation (high in symbionts, low in symbiont-free cells) is consistent with the transfer of newly fixed nitrogen from its source in symbionts to its inclusion in host cellular pools. These results provide strong evidence that newly fixed nitrogen is used by shipworm cells for biosynthesis (Fig. 4B).

MIMS technology has allowed us to localize, quantify, and compare nitrogen fixation in single cells and subcellular structures. We have demonstrated nitrogen fixation by individual symbiotic bacteria and have provided strong evidence of its use by the host. This symbiotic strategy is reminiscent of symbioses proposed to occur in the root nodules of leguminous plants and may explain the unusual ability of *L. pedicellatus* to

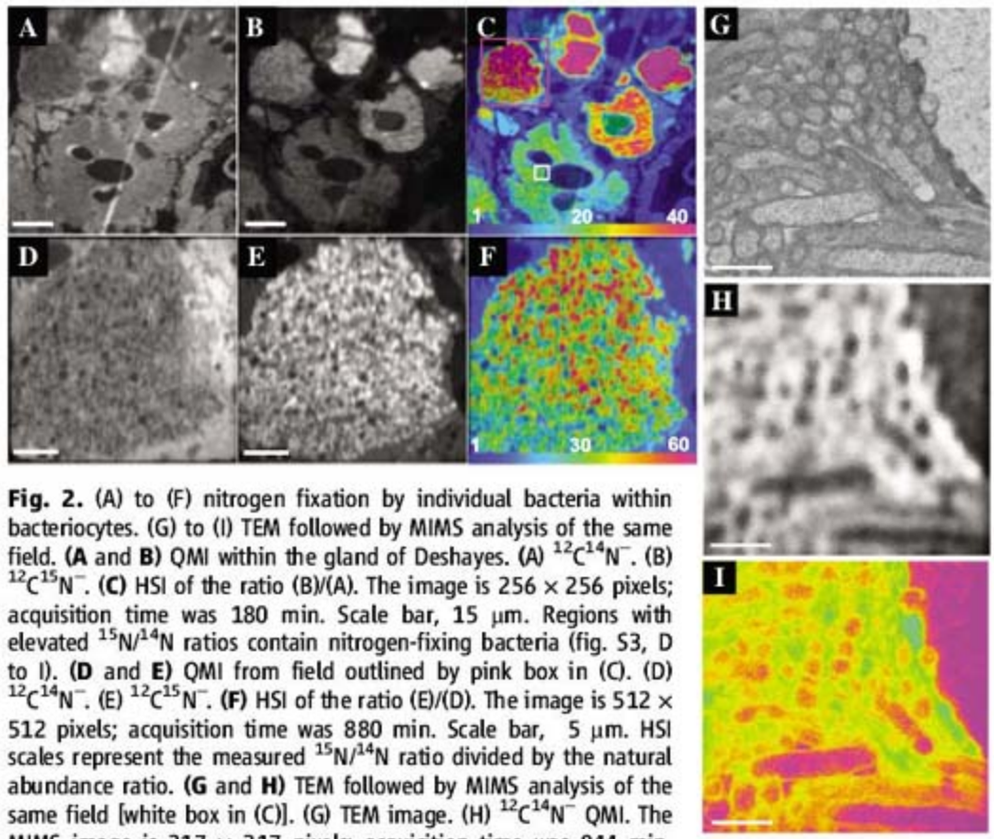


Fig. 2. (A) to (F) nitrogen fixation by individual bacteria within bacteriocytes. (G) to (I) TEM followed by MIMS analysis of the same field. **(A** and **B)** QMI within the gland of Deshayes. (A) $^{12}C^{14}N^-$. (B) $^{12}C^{15}N^-$. **(C)** HSI of the ratio (B)/(A). The image is 256 × 256 pixels; acquisition time was 180 min. Scale bar, 15 μm. Regions with elevated $^{15}N/^{14}N$ ratios contain nitrogen-fixing bacteria (fig. S3, D to I). **(D** and **E)** QMI from field outlined by pink box in (C). (D) $^{12}C^{14}N^-$. (E) $^{12}C^{15}N^-$. **(F)** HSI of the ratio (E)/(D). The image is 512 × 512 pixels; acquisition time was 880 min. Scale bar, 5 μm. HSI scales represent the measured $^{15}N/^{14}N$ ratio divided by the natural abundance ratio. **(G** and **H)** TEM followed by MIMS analysis of the same field [white box in (C)]. (G) TEM image. (H) $^{12}C^{14}N^-$ QMI. The MIMS image is 317 × 317 pixels; acquisition time was 844 min. Scale bar, 1 μm. **(I)** Overlay of (G) on (H). Note the excellent registration of the TEM and MIMS images.

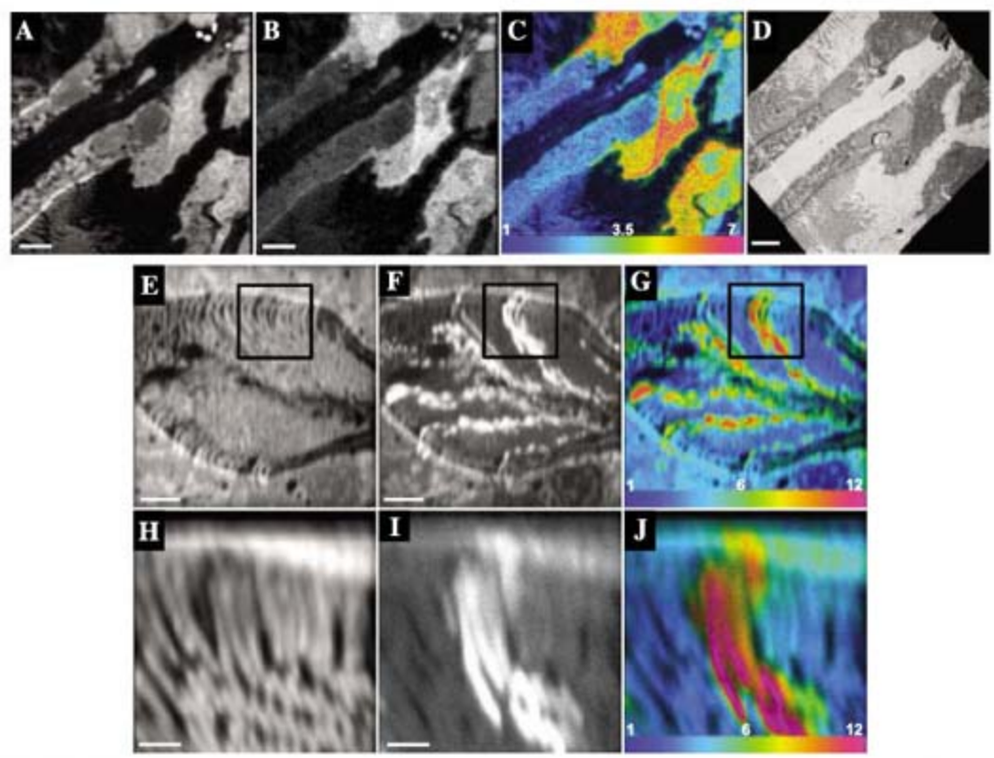
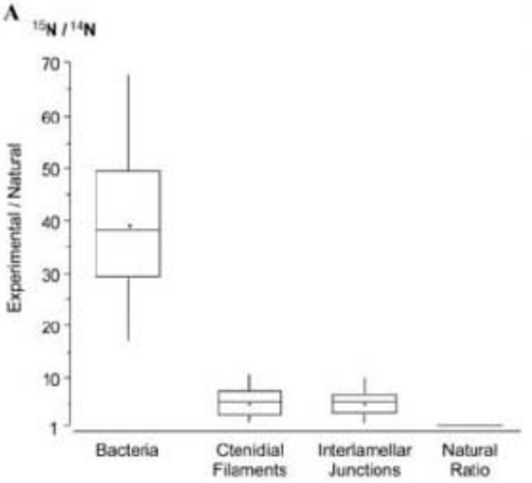


Fig. 3. Newly fixed nitrogen in bacteria-free regions of *L. pedicellatus*. **(A** and **B)** QMI of a ctenidial filament. (A) $^{12}C^{14}N^-$. (B) $^{12}C^{15}N^-$. **(C)** HSI of the ratio (B)/(A). The image is 256 × 256 pixels; acquisition time was 200 min. Scale bar, 5 μm. **(D)** TEM of a section consecutive to (A) to (C). Scale bar, 5 μm. **(E** and **F)** QMI of a lateral cilium. (E) $^{12}C^{14}N^-$. (F) $^{12}C^{15}N^-$. **(G)** HSI of the ratio (F)/(E). The image is 512 × 512 pixels; acquisition time was 880 min. Scale bar, 3 μm. **(H** and **I)** QMI of the area boxed in (E) to (G). (H) $^{12}C^{14}N^-$. (I) $^{12}C^{15}N^-$. **(J)** HSI of the ratio (I)/(H). The image is 512 × 512 pixels; acquisition time was 880 min. Scale bar, 1 μm. HSI scales represent the measured $^{15}N/^{14}N$ ratio divided by the natural abundance ratio. Note the elevated $^{12}C^{15}N/^{12}C^{14}N$ ratios in bacteria-free cells and cilia.

Table 1. ^{15}N incorporation in *L. pedicellatus* expressed as the experimental/terrestrial $^{15}N/^{14}N$ ratio.

	N	Mean	SD	Maximum	Minimum
Bacteria within bacteriocytes	1863	39.1	11.9	67.9	17.1
Ctenidial filaments	254	5.44	2.67	11.0	1.39
Interlamellar junctions	152	5.31	2.02	9.81	1.53



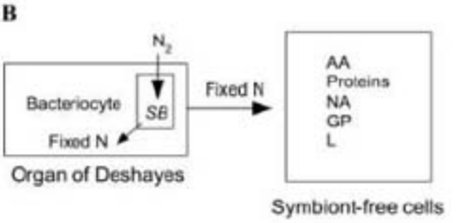


Fig. 4. Incorporation of ^{15}N by bacteria in bacteriocytes and nitrogen use by symbiont-free tissues. **(A)** Box plots of the $^{12}C^{15}N/^{12}C^{14}N$ isotope ratios within the bacteriocytes and in symbiont-free cells (see box plot description in fig. S4 legend). **(B)** Cartoon of proposed nitrogen fixation and transport in *L. pedicellatus*. Nitrogen diffusing from seawater into the gill tissue is fixed by symbiotic bacteria (*SB*) in the gland of Deshayes, then transported away and diluted into the host's biomass pool, providing nitrogen for synthesis of amino acids (AA), proteins, nucleic acids (NA), glycoproteins (GP), and compound lipids (L) used for host tissue metabolism.

survive and grow on a nearly nitrogen-free diet of wood (*27*) (Fig. 4B). Thus, this work suggests a function for the shipworm/bacteria symbiosis that has not been demonstrated previously for any other animal endosymbiosis: the conversion of nitrogen from atmospheric gas into animal biomass. This method, which also can be applied to measure the distribution of any stable (or radioactive) isotope-labeled molecule at micrometer to nanometer scales, provides a template for the study of individual microbes in a population and of their roles in the physiology, pathology, and ecology of life.

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Supporting Online Material

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Materials and Methods
SOM Text
Figs. S1 to S5
Table S1
References

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10.1126/science.1145557

Real-Time Cell Monitoring

The ECIS 9600 is a high-throughput instrument designed to monitor cells grown in special arrays having a standard 96-well plate configuration and footprint. Like other electric cell-substrate impedance sensing (ECIS) instruments, it uses a very weak AC current to measure the impedance of a small active electrode in each well in real time to provide nearly immediate indications of cell activity and response to agents. The consumable 96-well arrays are easily connected to the instrument using a single lever to make electrical contact. The instrument is capable of scanning all 96 wells in approximately 30 seconds (with three AC frequencies available). In addition to noninvasive measurements, the ECIS 9600 can be programmed to apply elevated fields for cell migration measurements via an automated wound-healing assay. The same high fields can also be used at shorter duration to electroporate membrane-impermeable compounds into cells for analysis. Data acquisition and analysis is handled by user-friendly software running on a Windows XP Professional platform, with data readily converted to text files for export. In addition to cell migration, assays can be devised for applications in signal transduction, cell invasion, and in vitro toxicology.

Applied BioPhysics For information 866-301-3247 www.biophysics.com

Workstation

The Carousel 6 reaction station is for individual chemists who require ease of use, operational versatility, and productivity in a benchtop synthetic workstation. The Carousel 6 provides chemists with a simple and convenient tool that can be configured to simultaneously stir up to six reactions at −70°C to +180°C, in a range of round-bottomed flasks from 5 ml to 250 ml. Drop-in aluminum inserts provide the flexibility for different sizes of reaction flasks to be used in a single system. An integral reflux head with central gas inlet and radial distribution system, combined with gas-tight PTFE caps, allows reactions to be carried out under an inert atmosphere. The affordability of the Carousel 6 brings the productivity benefits of parallel synthesis to individual chemists at a fraction of the cost of comparable systems. Its small footprint requires a minimum of fume cupboard space. It offers a cooling reservoir option that is compatible with a wide range of freezing mixtures.

Radleys For information +44 1799 513320 www.radleys.com

Uniform Magnetic Microspheres

The ProMag magnetic microspheres are polymer-based, highly uniform beads. Their surface chemistry and surfactant-free preparation offer easy attachment of ligands for many applications in the life sciences. Rapid separation rates make them suitable for automated assay systems or benchtop use.

Polysciences For information 800-523-2575 www.polysciences.com

RNA from a Single Cell

The ArrayPure Nano-scale RNA Purification Kit provides all the reagents needed to purify RNA from one or more eukaryotic cells, including quantities typically obtained with laser capture procedures. The kit contains only aqueous solutions and requires no toxic organic solvents. A nano-scale protocol has been developed and tested with quantitative real-time polymerase chain reaction on 1 to 10,000 eukaryotic cells. ArrayPure is also compatible with RNA amplification techniques in which microgram amounts of RNA have been produced from 20 HeLa cells.

Epicentre Biotechnologies For information 800-284-8474 www.EpiBio.com/arraypure.asp

Microscope with LED Illumination

The Leica DM1000 LED microscope features long-lasting light-emitting diode (LED) illumination, which provides color-neutral illumination and rarely needs lamp replacement. An optional, portable solar power supply is available for field-based applications. LEDs offer long service life, low heat generation, and low power consumption. Ergonomic features include height-adjustable focus button and eye tubes that can be individually adjusted or configured with an ergonomic 15° viewing angle. The microscope features a hard ceramic stage that can withstand years of use.

Leica Microsystems For information +49 6441 29 2550 www.leica-microsystems.com

Therapeutic Protein Generation

The OptiCHO Express Kit is designed to quickly produce high yields of therapeutic proteins from CHO DG44 cells. The 10-reaction kit comes complete with a detailed protocol, cloning vector, reagents, cells, and media all optimized to work together. The kit allows users to transfect CHO DG44 cells in a serum-free environment, as well as rapidly develop stable, high expression cell lines. CHO DG44 cells are a key bioproduction cell line. Because they lack dihydrofolate reductase, when transfected with the right vectors, they can be made to produce excess protein.

Invitrogen For information 716-774-6737 www.invitrogen.com/bioproduction

High-Throughput Laser Microdissection

The PALM CapturePlate 96 is a microtiter plate designed to bring high throughput to laser microdissection. Up to 96 specimens—isolated tissue areas or cells removed from a tissue sample—can be taken directly from glass slides without any manual intermediary step. The specimen is obtained contamination-free through the use of the unit's laser microdissection and pressure catapulting (LMPC) technology. The specimens can be distributed precisely among the individual wells through the use of the PALM RoboMover capture unit.

Carl Zeiss For information +49 (0) 3641 642770 www.zeiss.de

Literature

Automating Kinetic Fluorescence Whole Cell Assays Using the Velocity11 BioCel Screening Platform is a technical poster that describes how a labor-intensive, multi-step assay was automated, providing time savings and enhanced assay consistency. Kinetic fluorescence whole cell assays are widely used in high-throughput screening laboratories, but automating them has been a challenge. These assays frequently involve wash steps and multiple plate additions and ideally should be prepared entirely at 37°C. The poster describes a protocol for performing the entire process in a controlled environment.

For information +44 1763 269110 wwww.velocity11.com

Newly offered instrumentation, apparatus, and laboratory materials of interest to researchers in all disciplines in academic, industrial, and government organizations are featured in this space. Emphasis is given to purpose, chief characteristics, and availability of products and materials. Endorsement by *Science* or AAAS of any products or materials mentioned is not implied. Additional information may be obtained from the manufacturer or supplier.

FACULTY POSITIONS

BIOLOGICAL CHEMISTRY FACULTY POSITION
Wayne State University

The Department of Chemistry at Wayne State University seeks applications for a tenure-track position in the Division of Biological Chemistry. Preference will be given toward candidates at the **ASSISTANT PROFESSOR** level. Candidates must have a Ph.D. and the potential to develop a nationally recognized, externally funded research program of outstanding quality in any area of biological chemistry. The Department offers exciting opportunities for candidates with research interests complementing a large group of faculty working in the areas of DNA, RNA and protein biochemistry, enzymology, carcinogenesis, biophysical, bioorganic, and bioinorganic chemistry, as well as molecular and cellular biology (see departmental **website: http://chem.wayne.edu** for further information).

The Department of Chemistry has a supportive academic environment and a strong graduate program. Excellent opportunities exist for collaborative research with individuals in the Department of Biological Sciences, the basic science departments in the highly ranked School of Medicine, the College of Pharmacy and Health Sciences, as well as in the Center for Molecular Medicine and Genetics, the Institute for Environmental Health Sciences, and the Barbara Ann Karmanos Cancer Institute. The Department of Chemistry offers an excellent research environment that includes ample, newly renovated research laboratories and a fully staffed Central Instrument Facility that manages state-of-the-art equipment for: electrospray ionization and MALDI-TOF mass spectrometry, circular dichroism, electron parametic resonance, surface plasmon resonance, transmission electron microscopy, and nuclear magnetic resonance (NMR) (including a 700 megahertz [MHz] NMR with cryoprobe). The Wayne State faculty also have access to the resources of the Michigan Core Technology Alliance **(website: http://www.ctaalliance.org/),** which includes facilities for bioinformatics, proteomics, genomics, animal models and structural biology, including 900 MHz NMR and a dedicated synchrotron beamline for X-ray crystallography.

Applicants should submit a complete resume and description of future research plans, as well as three letters of recommendation addressing both research and teaching potential. All materials should be sent to: **Professor Charles H. Winter, Associate Chair, 141 Chemistry, Wayne State University, 5101 Cass Avenue, Detroit, MI 48202-3489.** In addition to the materials noted above, applicants must complete an online application at **website: https://jobs.wayne.edu.** Please apply for all chemistry faculty positions listed. Review of applications will begin in October 2007. *Women and minority candidates are encouraged to apply. Wayne State University is an Equal Opportunity and Affirmative Action Employer.*

ACADEMIC SURGICAL PATHOLOGIST. Tufts-New England Medical Center, Boston, Massachusetts. The Department of Pathology, Tufts-New England Medical Center, invites applicants for an academic surgical pathology position at the rank of **ASSISTANT/ASSOCIATE PROFESSOR.** Applicants must be board certified in anatomic and clinical pathology and hematopathology with additional subspecialty experience in renal pathology. The position will involve active participation in diagnostic surgical pathology including cytopathology as well as commitment to existing basic research programs in animal models of immune-mediated kidney disease. Responsibilities also include teaching of medical students at Tufts University School of Medicine. A strong record of academic achievement and publications is required. Please forward curriculum vitae, a brief statement of recent interests and the names of three references to: **Stephen P. Naber, M.D., Ph.D., Pathologist-in-Chief, Department of Pathology, Tufts-New England Medical Center, NEMCH #802, 750 Washington Street, Boston, MA 02111.**

FACULTY POSITIONS

THE UNIVERSITY of TENNESSEE HEALTH SCIENCE CENTER

CHAIR
Department of Anatomy and Neurobiology

The University of Tennessee Health Science Center College of Medicine seeks a diverse pool of nominees and applicants for the position of the Simon R. Bruesch Professor and Chair of the Department of Anatomy and Neurobiology (website: http://www.utmem.edu/anatomy-neurobiology/). The University of Tennessee Health Science Center is committed to excellence in education, research, and service. The Department of Anatomy and Neurobiology is currently home to 25 full-time faculty members, 27 secondary appointees, and 17 graduate students, most of whom participate in the campuswide Neuroscience Institute (website: http://www.utmem.edu/neuroscience/), which includes over 80 neuroscience faculty. The Department Chair will lead the recruitment of several tenure-track faculty to expand the Department in modern research laboratories. Applicants should have a demonstrated commitment to and knowledge of Equal Employment Opportunity and Affirmative Action.

The Department Chair will have distinguished accomplishments and national recognition in neuroscience research, experience in graduate and medical student education, and experience mentoring junior faculty. Candidates must possess a Ph.D. degree or equivalent, or an M.D. degree in an appropriate scientific discipline. The position requires proven leadership abilities establishing productive collaborations with other basic and clinical science department leaders. The successful candidate will be capable of providing energetic leadership and should be able to articulate a vision for continued growth and development of a major Anatomy and Neurobiology Department that currently ranks among the top programs in the country. Qualified applicants must submit a letter of interest accompanied by curriculum vitae and the names and addresses of three references to: **William Pulsinelli, Ph.D., M.D. Semmes Murphey Professor and Chair, Department of Neurology Chair, Anatomy and Neurobiology Chair Search Committee, The University of Tennessee Health Science Center, P.O. Box 63647, Memphis, TN 38163.** Review of applicants will begin immediately and will continue until the position is filled. *The University of Tennessee is an Equal Employment Opportunity/Affirmative Action/Title VI/Title IX/Section 504/ADA/ADEA Institution in the provision of its education and employment programs and services.*

PLANT ECOLOGIST. North Central College invites applications from broadly trained Plant Ecologists for a tenure-track appointment. Ph.D. required, postdoctoral experience preferred. Teaching assignments include courses in ecology, botany, and environmental science as well as our introductory biology sequence. Applicants should exhibit a potential for excellence in undergraduate teaching and mentoring, as well as a commitment to scholarship that includes collaborative research with undergraduates and an interest in contributing to an interdisciplinary general education program. Review begins on November 9, 2007. See **website: http://www.noctrl.edu/biology** for more information. Applicants who would enrich the diversity of the campus community are strongly encouraged to apply. *Equal Opportunity Employer.*

MAKE WAY FOR THE NEXT GENERATION:
JUNIOR FACULTY ARE MOVING IN

Universities across the United States and Europe are increasingly reshaping recruitment policies in order to attract and retain more junior faculty. Replacing the old sink or swim attitude is a desire to provide a more supportive and nurturing environment. Driving the new trend are several factors, including a concern that many of today's senior faculty are approaching retirement age and will need to be replaced, and a desire to have faculty that more closely reflect the gender and ethnic diversity of the population they serve. **By Julie Clayton**


Debra Auguste

Private universities such as Harvard, Yale, and Princeton have historically hired more at senior levels—tending to hire the most distinguished scholars they could find. Junior faculty would be hired for three to six years and then had to move elsewhere. That has changed a bit, and they tend to be hiring more junior faculty now,which includes efforts to recruit women and minorities into the sciences." These are the words of **Bob Berdahl,** president of the American Association of Universities (AAU), describing what appears to be a widespread shift in the hiring paradigm for junior level faculty in the United States.

The Aging Work Force

When **Debra Auguste** decided to leave Princeton last year for a position at Harvard University, it was because Harvard today is attempting to move away from its past reputation for failing to support junior faculty. Taking up the post of assistant professor in the Harvard School of Engineering and Applied Sciences, Auguste has been given every encouragement to consider this as a place to establish her long-term research career, with a good chance of obtaining tenure.

"They really are pushing to develop junior faculty and they're investing a lot in each and every one of us," she says. The investment included a generous startup package—a custom-designed laboratory of around 1,600 square feet for the study of embryonic stem cells and tissue engineering. "Everything was put into place to be as I designed it. If I don't succeed, it rests on my own shoulders."

> "They really are pushing to develop junior faculty and they're investing a lot in each and every one of us."

Another new recruit is Hopi Hoekstra, who moved from the University of California, San Diego to become an associate professor in the Harvard Department of Organismal Biology—a tenure-track position that will be reviewed after three years. Hoekstra studies ecological genetics with wild mouse populations, trying to understand how changes in DNA can alter fitness and survival. She brought a total of five students and postdocs from California, and has recruited an additional five since arriving last year.

Like Auguste, Hoekstra credits the "amazing resources" and "incredibly supportive environment" as the key attractions of Harvard, including a newly established junior faculty mentoring program. "I really feel like senior faculty are amazing mentors. They've had to go through the process and scientifically they're strong."

"Historically, Harvard has the reputation that it doesn't treat faculty well—that it's hard to get tenure. Harvard would more often appoint a senior person, a leader in their field, and junior faculty did not measure up. says **Andrew Biewener,** chair of the Department of Organismal Biology where Hoekstra is based. "But the view we take now is that it's the younger people in the faculty who are most likely to be doing cutting-edge research. We're trying to hire the best, who will advance in their careers and receive tenure, in our department and in the life sciences generally."

The Retirement Boom

Harvard's sizable endowment enables it to put financial muscle behind continued »

CREDIT: ELIZA GRINNELL

UPCOMING FEATURES

International Careers: Germany — September 21

Careers and Grad. Programs — September 28

Focus on Diversity — October 5

Faculty Positions

"We're continually growing. We're so big and we recruit so much that [the aging work force] is not a significant issue for us."
—Alan Fogelman

these changes, but publicly funded universities also seem to be improving the prospects for junior faculty. For some institutions, this may prove critical for survival, especially given the expected retirement of many senior faculty over the next decade.

At the University of North Carolina, Chapel Hill, for example, the faculty retirement rate is predicted to double over the next 10 years, with at least 500 faculty retiring. This is the cohort of faculty born during the postwar baby boom era of the 1950s and 1960s, who joined expanding university faculties during the 1970s. "It was an unprecedented time of growth and hiring. And that means we have a very large bolus of faculty members moving up the age scale," says UNC associate vice chancellor for research and economic development, **Bob Lowman.**

Lowman has recently compiled a report for UNC's vice chancellor on the future of UNC's faculty, using statistics from the National Science Foundation as well as those of UNC. He warns that UNC will need to recruit "unprecedented numbers of new faculty members at the same time as other American universities will be trying to do the same."

The problem of retiring faculty is compounded by a high proportion of temporary staff to tenured faculty, hired to do the "heavy work" on large interdisciplinary projects, according to Lowman. This means that despite a 30 percent rise in faculty numbers over the past 10 years, the number of tenure-track positions at UNC has dropped by 4 percent. The result is a "two-tiered system of faculty" in which fixed-term faculty have no right to tenure, and can continue for up to 20 years with their salaries dependent on grants.

While this may be good for research, Lowman cautions that when the predicted mass retirement among faculty takes place, there may not be sufficient numbers of tenure-track faculty to replace them, and those on fixed-term contracts may go for tenure elsewhere.

"There is concern among a lot of institutions about the aging of the faculty," notes Berdahl of the AAU. He points to the recent removal of mandatory retirement at the age of 65 in the United States as an additional factor, encouraging more workers to postpone retirement.A delay in retirement can impede the appointment of new junior faculty. At Harvard, "Senior science faculty tend not to retire—they stay on for as long as possible, and this creates a problem in the demographics. We need to make sure they see advantages in retiring at a reasonable time. That's a challenge." notes Biewener.

University of California, Berkeley, where Berdahl was chancellor, tackles the problem by using special funds to promote early retirement among senior faculty, permitting them to continue doing research part time and some teaching. "The virtue for the institution is that it frees up some of the salary. This is becoming more common practice and encourages universities to hire junior faculty," says Berdahl. He adds that recruitment of junior faculty is often preferred nowadays because it tends to be less expensive than recruiting senior faculty – who "tend to bargain for more startup costs."

Other institutions are confident that they will remain successful even if competition intensifies in future. The UCLA Department of Medicine, for example, which has more than 600 faculty members working across two hospitals, in Westwood and Santa Monica, California, has seen its research funding grow from an annual turnover of $22 million in 1992 to more than $125 million this year. "We're continually growing. We're so big and we recruit so much that [the aging faculty work force] is not a significant issue for us. There won't be any vacancies," says **Alan Fogelman,** director of the Specialty Training and Advanced Research (STAR) program, and executive chair of the Department of Medicine.

The STAR program ensures a smooth entry of highly qualified physician-scientists into UCLA faculty, by offering tenure-track positions to selected medical school graduates in which they can undergo rigorous scientific training at they same time as doing their clinical residencies. It enables graduates who would not otherwise have chosen this path to realize their interest in science at a later point. "Along the way they get bitten by the science bug and want to do research." says Fogelman.

Since 1994 there have been 72 graduates from the program, awarded either Ph.D.s or Masters in clinical bioscience, with the majority choosing to remain in research. Half have gained positions as either clinical instructors or assistant professors at UCLA, with the possibility of becoming fully tenured associate professors upon evaluation, while the remainder have gone on to successful positions all over the world, mostly in research.

American Association of Universities
www.aau.edu

Brown University
www.brown.edu

Department of Organismal Biology
www.oeb.harvard.edu

Harvard University
www.harvard.edu

Museum of Comparative Zoology
Harvard University
www.mcz.harvard.edu

STAR Program, UCLA
www.star.med.ucla.edu

University of Kentucky
College of Arts and Sciences
www.as.uky.edu

University of North Carolina
Chapel Hill
www.unc.edu

University of Sheffield, UK
www.sheffield.ac.uk

Universities UK
www.UniversitiesUK.ac.uk

The European Perspective

These initiatives are not occurring only in the United States. In the UK, for example, there also is an increasing recognition that the career paths of junior researchers need to be better established, with more support for gaining tenure. The Academic Fellowships program run by Research Councils UK (the umbrella organization that disburses government funds of £3 billion to university-based research) aims to achieve this. The program, started in 2005, provides five years of funding to promising postdoctoral researchers and a guarantee of tenure. This can also include a six-month sabbatical to spend in a laboratory elsewhere.

One recipient is **Bram Snijders,** originally from The Netherlands, who continued »

Masdar Institute of Science and Technology, Abu Dhabi, UAE
Professors
Associate Professors
Assistant Professors

The Masdar Institute of Science and Technology (Masdar Institute), with the assistance and advice of the Massachusetts Institute of Technology (MIT), is being founded as a new and independent non-profit, tax-exempt research and educational institution (initially at the graduate level) dedicated to premier engineering research and education. The goal of the Institute is to develop, over a period of years, indigenous R&D capacity in Abu Dhabi, addressing issues of importance to the region in critical areas such as: renewable energy, sustainability, environment, water resources, and systems engineering and management, as well as to provide qualified men and women in the region with the opportunity to obtain graduate degrees in these technical fields.

Job Responsibilities: Teach graduate courses, supervise master and doctoral students, develop a research program and seek external funding for such research, and participate in the Institute's service and outreach activities.

Qualifications: The Masdar Institute is seeking applicants for Professor, Associate Professor, and Assistant Professor in the fields of Water Resources and the Environment, Engineering Systems and Management, and Information Technology. Applicants should have a strong record of published research, experience in supervising graduate students, and relevant teaching experience. The applicant must be fluent in English. An earned doctorate in the relevant field is required. Relevant non-academic work experience would be an advantage.

Positions in Water Resources and the Environment: Faculty will provide research leadership and educational activities to engineering and science students concerned about the future of water supply and use, as well as an understanding of environmental systems. Specialists from Civil, Environmental, Mechanical and Chemical Engineering are encouraged to apply, as well as faculty from other disciplines such as Chemistry, Materials Science, Biological Engineering, Electrical Engineering, Biology, and Nanotechnology, whose advanced scientific work may have implications for water and the environment, even if they have not directly worked in the water and environmental area. Candidates specializing in the area of desalination and advanced water reuse in such areas as polymer membranes, ceramic membranes, biological filtration and new oxidation techniques will be considered, as well as experts in environmental systems methods such as life cycle analysis and in environmental sciences focused on fate and transport of pollutants in the environment and the mitigation and remediation of the impacts of new water and environment technologies.

Positions in Engineering Systems and Management: The Engineering Systems and Management program will provide intellectual research leadership and educational activities to students interested in applying a systems approach to the engineering and management of renewable and sustainable energy technologies. The Institute is looking for candidates in one of the following areas: Operations Research (Stochastic Modeling, Optimization, Decision Science, Simulation), Operations Management (Manufacturing, Technology Innovation) and Industrial Economics (Industrial Organization, Technology Policy, Economic Development).

Positions in Information Technology: Faculty candidates must be capable of teaching and conducting research in such IT areas as: Software Engineering; Information Processing for Engineering Systems; Database, Internet, and Systems Integration Technologies; Data Mining; Artificial Intelligence and Semantic Web; Communications and Connectivity among Information Systems; Information Management; Intelligent Systems; and Pervasive Computing. In addition, faculty are expected to effectively collaborate with other faculty areas such as Water Resources and the Environment, Materials Science and Engineering, Mechanical Engineering and Engineering Systems and Management.

Application Submittal Information: The Massachusetts Institute of Technology is assisting the Masdar Institute in the search. Initial screening of applications will begin immediately. Application deadline is **October 30, 2007**. Application materials should include your name, address, telephone numbers, curriculum vitae and what specific position you are applying for, your current position, a description of how your experience matches the position requirements, and e-mail contact information for three references.

Materials should be submitted electronically as a MS Word attachment to:

Dr. Russel Jones, President
Masdar Institute of Science and Technology, Abu Dhabi, United Arab Emirates
Co-Chair, Search Committee for Masdar Institute of Science and Technology
e-mail: rjones@masdar.ae

Copy to:
Dr. Fred Moavenzadeh, Co-Chair
Search Committee for Masdar Institute of Science and Technology
c/oTechnology and Development Program
Massachusetts Institute of Technology
e-mail: tdpmail@mit.edu

BIOLOGY

THREE TENURE-TRACK BIOLOGY FACULTY POSITIONS

Physiology, Genetics, & Biology Education/Pedagogy

The Department of Biology at The College of New Jersey (TCNJ) invites outstanding applicants for three tenure-track faculty positions, starting August 2008. Teaching and research are mutually supportive activities at TCNJ. Candidates should be strongly committed to the teacher-scholar model in a primarily undergraduate, residential institution and to maintaining both high quality teaching and an active and productive research program involving highly motivated undergraduates. Faculty members also serve as academic advisors and have service responsibilities within the College. A research laboratory and competitive start-up funds will be provided. The Biology Department is housed in a modern biology building (opened Fall 2000) that offers state-of-the-art teaching and research facilities and instrumentation.

We seek broadly trained candidates who also have potential to collaboratively contribute to interdisciplinary curricular and scholarly efforts within the School of Science and at the College. In addition to the courses listed below, teaching responsibilities may include rotation through either majors and/or non-majors introductory courses. Candidates should have a Ph.D. and post-doctoral experience is preferred.

✳ **Physiology** *(Assistant Professor)*

To develop and teach a junior/senior-level course in animal physiology, an upper level course in area of specialty, and one of our core courses. The candidate will not be expected to teach courses in human anatomy and physiology. Research in any area of physiology will be considered.

✳ **Genetics** *(Assistant Professor)*

To teach a core course in genetics and an upper-level course(s) in area of specialty. Research in any area of genetics will be considered.

✳ **Biology Education/Pedagogy** *(Assistant or Associate Professor)*

To teach an interdisciplinary science course to elementary education majors, teach content courses to biology majors preparing for secondary teacher certification, teach an upper-level course in area of specialty, conduct research in the area of biology education/pedagogy, and provide leadership in emerging undergraduate science education initiatives and funding opportunities.

To apply, send a letter of application, current curriculum vitae, statement of teaching philosophy, statement of research interests and goals, representative publications, all graduate and undergraduate transcripts, and three letters of recommendation to:

Faculty Search (indicate position), Department of Biology
The College of New Jersey, PO Box 7718, Ewing, New Jersey 08628-0718

All materials must be received as hard copies in postal mail. **Review of applications will begin October 8, 2007.**

For further information about our program, please visit: http://www.tcnj.edu/~biology/

TCNJ The College of New Jersey

AA/EOE

BOSTON UNIVERSITY MEDICAL CAMPUS

Boston University School of Medicine welcomes applications for its departments & programs below at ranks of Instructor, Assistant & Associate Professor, or Professor. Email a cover letter specifying your department or interest area with your CV to **busmdean@bu.edu**. Boston University is an equal opportunity and affirmative action employer

Departments:

- **Anatomy and Neurobiology**
- **Biochemistry**
- **Genetics and Genomics**
- **Microbiology**
- **Physiology and Biophysics**
- **Pharmacology & Experimental Therapeutics**
- **Pathology**

Interest areas:

- **Immunology**
- **Structural, cell or cancer biology**
- **Neurosciences**

Faculty Recruiting

The Jackson Laboratory

The Jackson Laboratory, a mammalian genetics research institution, and an NCI designated Cancer Center, has launched a major research expansion. Faculty members, especially those with a focus in cancer, will be recruited in the following areas:

- **Computational Biology/Bioinformatics**
- **Immunology/Hematology**
- **Metabolic Disease Research**
- **Neurobiology**
- **Reproductive/ Developmental Biology**

We encourage applications for positions at the **Assistant, Associate** and **Full Professor** level, especially from those with an interest in interdisciplinary and/or translational approaches. Candidates should have a Ph.D., M.D., or D.V.M., and have completed postdoctoral training with a record of research excellence, and they must have the ability to develop a competitive, independently funded research program that takes advantage of the mouse as a genetic model for human development and disease.

We offer a unique scientific research environment, including excellent collaborative opportunities within our faculty of 37 principal investigators, unparalleled mouse genomic resources, outstanding core scientific support services, highly successful postdoctoral and predoctoral training programs, and a major scientific meeting center, featuring courses and conferences centered on mouse models.

For more information, go to: www.jax.org

Applicants should send a curriculum vitae and a concise statement of research interests and plans, and arrange to have three letters of reference sent to: **facultyjobs@jax.org**
Review of applications will begin in January of 2008.

The Jackson Laboratory is an EOE/AA employer.

The Jackson Laboratory, 600 Main Street, Bar Harbor, Maine 04609

www.jax.org

Faculty Positions
Department of Neurobiology
Yale University School of Medicine
New Haven, Connecticut

The Department of Neurobiology at Yale University School of Medicine has recently expanded as part of its strategic plan and is currently seeking to recruit two new tenure-track faculty positions at the assistant, associate, and professor levels. We seek outstanding scientists with strong records of accomplishments in Neuroscience. We are particularly interested in applicants actively investigating forebrain function and/or development using molecular, cellular, imaging, and/or electrophysiological techniques.

Successful candidates are expected to develop significant independent externally funded research, have a strong commitment to graduate and medical education, and participate in interdisciplinary departmental training grant and research programs/centers.

Interested applicants must have a Ph.D. and/or M.D. degree as well as postdoctoral experience with a proven record of productivity. Submit curriculum vitae, statement of research interests, and names of three references by **December 1, 2007** to:

Pasko Rakic, M.D., Ph.D.
Chairman, Department of Neurobiology
Yale University School of Medicine
P.O. Box 208001
New Haven, CT 06520-8001

Yale is an Affirmative Action/ Equal Opportunity Employer.

came to the University of Sheffield in 2002 to do his Ph.D. in chemical engineering before taking up a postdoctoral position in the same department. He had to impress RCUK with far longer term research plans than would be expected for a routine three-year postdoc, but the reward was worth it.

"It is a good career path. I notice that a lot of my colleagues are worrying about what the next contract will be. It's easier for me to plan ahead for the future, in both my professional and my personal life. I'm trying to set up collaborations both within and outside the University of Sheffield."

Snijders will spend the first three years doing postdoctoral research funded largely by the Biotechnology and Biological Sciences Research Council (BBSRC), and then two years in transition, applying for grants as an independent investigator and training in other skills including public outreach, before taking up his tenured post in which he will spend 50 percent of his time teaching. In contrast, he sees colleagues either leaving academia for industry or lowering their ambitions altogether by applying for technician posts, for the sake of a permanent job.

As in the United States, there are fears in the UK that "the current level of retirement is not being matched by new recruitment and retention within particular disciplines," according to a report by RCUK. The UK research base is aging, with the proportion of academic staff aged over 50 increasing from 24 percent to 28 percent between the years 1999 and 2005. Certain disciplines fare worse than others, with more than 30 percent of mathematicians aged over 50. Added to this are concerns that overall academic staff numbers are declining in some disciplines such as chemistry and engineering. Underlying the recruitment problem is the increasing attraction—especially for those in senior posts—of higher salaries in the private sector.

Mission: Retention

For universities on both sides of the Atlantic, recruitment of junior faculty is but the first hurdle. Then comes the challenge of retention. One initiative that is gaining in popularity for retaining junior faculty is mentoring.

At Harvard, this is increasingly becoming a formal practice. "We're looking at better ways to mentor—such as through having shared discussions. Before now we viewed it as important but it was more informal. Now, having a more formal program means that we can evaluate how it should happen," says Biewener.

For Auguste, this has been an important activity. "I saw faculty who are pillars in their areas and I thought that they'd not want to reach out to me. But I've had some really generous offers. People were very open and willing to connect. I had not seen this for friends who are professors at other top universities," says Auguste.

Smaller universities too are developing new initiatives in order to boost their prospects for attracting and retaining more faculty. At Brown University, mentoring is one of several activities funded through a major grant of $3.3 million from the National Science Foundation under its nationwide ADVANCE program. The program is open to both men and women, but it is viewed as especially beneficial to the retention of women scientists and engineers, who have traditionally felt less supported.

"Smaller colleges tend to do more about faculty development. We're a small university but we're research intensive," says **Pamela O'Neil,** associate provost for policy and planning at Brown, and principal investigator of the ADVANCE project.

"Smaller colleges tend to do more faculty development"

—Pam O'Neil

Mentoring is also proving useful at UNC for helping new faculty to adapt—especially those recruited from outside the traditional fields of a particular department. At the School of Pharmacy, for example, "Before, most faculty did residencies and graduate programmes in pharmacy. Now we're recruiting molecular biologists and chemical biologists, chemists or engineers," says **Bob Blouin,** dean of the school.

To help them overcome potential barriers of coming from outside the profession, the School of Pharmacy has introduced a junior faculty mentoring program, now in its second year. "They find it a big attraction because they don't feel like they're in that all alone," says Blouin.

Plenty of Perks

Junior faculty can also look forward to other kinds of support, such as parental leave and a stopping of the "tenure clock" for those starting a family. This means that the time taken out to care for children is not included in the period over which junior faculty are evaluated for tenure. Two years ago, Princeton University and the University of Michigan became the first to offer this as an automatic right to any new parents. The trend is now spreading, and the same policy was adopted in June this year at the University of Kentucky. Already, the university is reaping rewards by attracting more women.

"We advertised this policy a lot this year, and of the last 35 new faculty recruits, 16 were women—one of the highest [proportions] we've had for many years," says **Leonidas Bachas,** associate dean for academic research in the University of Kentucky College of Arts and Sciences.

New faculty can also look forward to a new emphasis on developing their teaching as well as research skills. UNC sees this as an important way of meeting its mission for teaching and training the region's future scientific work force.

"Most of the public domain expects public universities to create manpower for new industries as communities transform from old to new economies," says Blouin.

Junior faculty have the enthusiasm that he believes is a key quality for teaching.

"Some of our best scientists are often our best teachers. We want to give them a forum to share that with their students and show their passion for their work," says Blouin. Although the additional support and perks will help, it is essentially this passion that will turn today's junior faculty into tomorrow's professors, department heads, and deans.

Julie Clayton, a freelance science writer and journalist, works out of Bristol, UK.

10.1126/science.opms.r0700038

CREDIT: ELIZABETH LOVE

UTMB
The University of Texas Medical Branch

Faculty Position for Research in Parkinson's Disease

The Department of Neurology at the University of Texas Medical Branch (UTMB) at Galveston, in partnership with the George and Cynthia Mitchell Center for Neurodegenerative Diseases, is seeking a physician-scientist for a tenure-track faculty position *with the John Sealy Chair for Parkinson's Disease Research*. Candidates with clinical and/or basic science research interests in Parkinson's disease are specifically sought. The center, directed by **Dr. Claudio Soto**, provides a rich research environment linking basic neurobiological and translational aspects of neurodegenerative diseases. The successful applicant will be appointed at a rank and salary commensurate with experience. The position offers an attractive start-up package that includes adequate research space, clinical research coordination supports, and access to state-of-the-art core facilities.

Endowed Chair Position for Clinical Research in Alzheimer's Disease

The Department of Neurology at the University of Texas Medical Branch (UTMB) at Galveston, in partnership with the Mitchell Center for Neurodegenerative Diseases, is seeking a physician-scientist for a tenure-track faculty position responsible for clinical research in Alzheimer's disease. Candidates with both clinical research expertise and basic science research interests in Alzheimer's disease are specifically sought. The Mitchell Center, directed by **Dr. Claudio Soto**, provides a rich research environment linking basic neurobiological and translational aspects of Alzheimer's disease and other neurodegenerative diseases. The successful applicant will be appointed at a rank and salary commensurate with experience and will be awarded the John Sealy Distinguished Chair for Clinical Research in Alzheimer's Disease. The position offers an attractive start-up package that includes adequate research space, clinical research coordination supports, and access to state-of-the-art core facilities. To apply, please send a C.V. and the names of four references to:

Tetsuo Ashizawa, MD
Professor and Chair
Department of Neurology
The University of Texas
Medical Branch
301 University Boulevard,
Galveston, TX 77555-0539
Email: teashiza@utmb.edu

UTMB is an Equal Opportunity/ Affirmative Action University that proudly values diversity. Candidates of all backgrounds are encouraged to apply.

BCM
Baylor College of Medicine

Tenure Track Faculty Position in Cognitive or Computational Neuroscience

The Department of Neuroscience at Baylor College of Medicine is continuing a major expansion of its program in cognitive neuroscience. This initiative includes hiring six new faculty members, the provision of five interactive 3.0 Tesla fMRIs dedicated exclusively to brain research and the development of the Computational Psychiatry Unit for the quantitative study of human behavioral brain disorders. The facilities and collaborative environment offer a unique opportunity for the study of individual and group behaviors, access to large and diverse populations of human subjects, outstanding computational expertise, one of the nation's leading programs in genetics and human genomics and a strong basic neuroscience research community. Candidates should have the Ph.D. and/or M.D. and postdoctoral training in an appropriate field. Research involving fMRI analysis of decision-making, social interaction or group dynamics utilizing computational and genomic approaches to study behavioral disorders is encouraged. Send *curriculum vitae* and statement of research interests electronically as a single PDF to: **friedlan@bcm.edu** and have hard copies of at least three letters of reference sent to: **Cognitive Position, Michael J. Friedlander, Ph.D., Professor and Chair, Department of Neuroscience and Director of Neuroscience Initiatives, Baylor College of Medicine, One Baylor Plaza, Suite S740A, Houston, TX, 77030** by **October 25, 2007**. Please visit our departmental website at **http://neuro.bcm.edu** for more information.

Tenure Track Faculty Position in Integrative Neuroscience

The Department of Neuroscience at Baylor College of Medicine is recruiting a tenure track Assistant Professor who utilizes advanced tools to investigate information processing in the nervous system at the cellular, network and/or organismal organization level. The successful candidate should have a Ph.D. and or M.D., postdoctoral experience and a record of accomplishment in the application of biophysical, imaging, computational and/or neurophysiological approaches to integrative aspects of nervous system function and behavior. Candidates with interests in the information processing properties of synapses or dendrites, neuronal-glial interactions, neuronal network dynamics or the neural basis of behavior are encouraged to apply. The Department of Neuroscience (**http://neuro.bcm.edu/**) is undergoing a major expansion, building on strengths in ion channel and receptor function, cellular imaging, synaptic plasticity, neuronal and glial signaling, sensory processing, cognitive and computational neuroscience. The position will provide a highly competitive allowance for laboratory start up support. Send *curriculum vitae* and statement of research interests electronically as a single PDF to **friedlan@bcm.edu** indicating Integrative Position on the email header. Have hard copies of at least three letters of reference sent to: **Integrative Position, Michael J. Friedlander, Ph.D., Professor and Chair of Neuroscience and Director of Neuroscience Initiatives, Baylor College of Medicine, One Baylor Plaza, Suite S740A, Houston, TX, 77030** by **October 25, 2007**.

Tenure Track Neuroscience Faculty Position in Brain Aging Supported by the Cynthia and George Mitchell Endowed Fund

Baylor College of Medicine is recruiting a tenure track Assistant or Associate Professor who utilizes tools of contemporary neurobiology to investigate fundamental mechanisms of brain aging including learning, memory and associated diseases such as Alzheimer's. Candidates who use animal models to study brain aging and/or dementias and who have a record of accomplishment in the application of molecular biological, genetic, imaging, neurophysiological and/or behavioral approaches to the study of the effects of aging on processes such as learning and/or memory are encouraged to apply. Candidates should have a Ph.D. and/or M.D. and postdoctoral experience. The candidate will have their primary faculty appointment in the Department of Neuroscience and be a member of the Mitchell Center for Brain Aging and Dementia and the Learning and Memory Research Center, with opportunities for affiliations with other departments and programs. The position will provide a competitive allowance for laboratory start up and ongoing support. Send *curriculum vitae* and statement of research interests electronically as a single PDF to **friedlan@bcm.edu** indicating Brain Aging Position on the email header. Have hard copies of at least three letters of reference sent to: **Brain Aging Position, Michael J. Friedlander, Ph.D., Professor and Chair of Neuroscience and Director of Neuroscience Initiatives, Baylor College of Medicine, One Baylor Plaza, Suite S740A, Houston, TX, 77030** by **October 25, 2007**. Please visit the Department of Neuroscience website at: **http://neuro.bcm.edu**.

Baylor College of Medicine is an Equal Opportunity/Affirmative Action and Equal Access Employer.

FACULTY POSITIONS

FACULTY POSITION, ECOTOXICOLOGY
Bren School, University of California, Santa Barbara

The Donald Bren School of Environmental Science and Management (**website: http:// www.bren.ucsb.edu**) invites applications for a tenure-track **ASSISTANT PROFESSOR** position, to start July 1, 2008. We seek a Scientist in ecotoxicology whose work is clearly relevant for environmental policy or management. Applicants should possess a Ph.D. or have completed all requirements for the degree by the appointment date.

The successful candidate will have interests in investigating the effects of chemical stressors on organisms in the context of ecological systems and in applying scientific research to issues of environmental management. We seek a person with a strong background and experience in empirically studying interaction mechanisms between stressors and organisms using innovative methods in molecular biology, chemistry, and ecology.

The ability to teach both advanced courses for Ph.D. students and courses on ecological effects of pollutants and ecological risk assessment for professional Master's-level students is desirable. The candidate will be expected to carry out an outstanding research program and to mentor Ph.D. and Master's students.

Preference will be given to candidates whose existing or emerging research is complementary with existing areas of emphasis within the school, including corporate environmental management, ecological sustainability, environmental economics, governance for sustainable development, and sustainable management of water resources.

The Bren School is a graduate school providing rigorous, multidisciplinary training in environmental science and management to Master's and Ph.D. students. The faculty is drawn from the natural sciences, engineering, social sciences, and management.

Send applications to: **Ecotoxicology Search Committee, Donald Bren School of Environmental Science and Management, University of California, Santa Barbara, CA 93106-5131; e-mail: ecotox@bren.ucsb.edu; fax: 805-893-7612.**

Electronic submission of the application as a single package is highly desirable and must include curriculum vitae, names of three references, a statement of research interests and teaching experience, and copies of up to five publications. Applicants should arrange to have three letters of reference e-mailed to the Search Committee. For fullest consideration, all materials should be received by November 20, 2007, although the position will remain open until filled.

The University of California is an Equal Opportunity/Affirmative Action Employer. We encourage all qualified applicants to apply, including minorities, women, and persons with disabilities. The School is especially interested in candidates who will contribute to the diversity and excellence of the academic community through research, teaching, and service.

The Department of Ecology, Evolution, and Organismal Biology (EEOB) at Iowa State University seeks to fill two tenure-track positions at the **ASSISTANT PROFESSOR** level, one in evolutionary/ecological plant biology and one in microbial ecology. The successful candidates will join a dynamic Department of 30 faculty who use integrative approaches that bridge disciplines and span multiple levels of biological organization. Applicants must have a Ph.D. in a biological science, and are expected to develop a nationally recognized research program and skillfully contribute to undergraduate and graduate teaching. Following the instructions on **website: http://www.iastatejobs.com,** submit cover letter, curriculum vitae, and research and teaching statements as a single PDF file not to exceed 1MB, plus up to three reprints as pdf files, each not to exceed 1MB, by 19 October 2007 (see **website: http://www.eeob.iastate.edu/search.html** for additional information).

In addition, arrange to have three letters of recommendation sent by e-mail as PDF files to **e-mail: searches@iastate.edu.** *ISU values diversity and is an Affirmative Action/Equal Employment Opportunity Employer with NSF ADVANCE funding to enhance the success of women faculty in science and engineering.*

FACULTY POSITION in TOXICOLOGY

The C. Eugene Bennett Department of Chemistry at West Virginia University, in support of expanding multidisciplinary efforts in biomedical, life, and forensic sciences, invites applications for an open-rank tenure-track position. The Department seeks applicants with research interests in the area of toxicology. Applicants must have a Ph.D. degree and postdoctoral experience is preferred for junior candidates. Excellence in teaching at the undergraduate (including forensic toxicology) and graduate levels is expected. The successful applicant will initiate and develop a vigorous research program using a competitive startup package and through acquisition of funds from federal sources such as the NSF, NIH, Department of Energy, and USDA. Ample collaborative opportunities exist locally in Health Sciences and National Institute for Occupational Safety and Health. Applicants should submit curriculum vitae, a description of research plans, a detailed startup budget, a brief description of teaching interests, and arrange for three letters of recommendation to be sent to: **Toxicology Faculty Search Committee, Bennett Department of Chemistry, P.O. Box 6045, West Virginia University, Morgantown, WV 26506-6045.** Applications can also be sent to **e-mail: chemistry@mail.wvu.edu.** Review of completed applications will continue until the position is filled, with priority given to applications received by November 15, 2007. *WVU is an Equal Opportunity/Affirmative Action Employer. Women and protected class individuals are encouraged to apply.*

ASSISTANT/ASSOCIATE PROFESSOR
University of Arkansas, Little Rock
Plant Molecular Biology

The Applied Science Department at the University of Arkansas at Little Rock is an interdisciplinary graduate department in engineering and sciences (**website: http://technologize.ualr.edu/appliedscience/**). The Department is soliciting applications for a tenure-track Assistant Professor (job #385) in the area of plant molecular biology. Appointment at the Associate Professor level is possible for candidates who have an externally supported research program and a substantial publication record. Candidates working in all areas of plant molecular biology will be considered. Applications are especially encouraged from candidates who generate and integrate complex data from biochemical, proteomic, and genomic studies. The successful candidate must establish a vigorous independent research program supported by external funding. We are particularly interested in candidates who will participate in collaborative interdisciplinary research, such as energy and environmental biosciences, bioengineering, or biomaterials. Candidates must have a Ph.D. in biology, biochemistry, molecular biology, or a closely related discipline.

To apply, applicants should send an application letter (job #385), curriculum vitae, a statement of research interests and teaching philosophy, and names and contact information of three references to: **Faculty Search Committee-Plant Molecular Biology, Department of Applied Science, University of Arkansas at Little Rock, AR 72204-1099. (Telephone 501-569-8000; e-mail: dgwhite@ualr.edu.)** Review of applications will begin November 2, 2007, and continue until the position is filled. *The University of Arkansas at Little Rock is an Equal Opportunity, Affirmative Action Employer and actively seeks the candidacy of minorities, women and persons with disabilities. Under Arkansas law, applications are subject to disclosure. Persons hired must have proof of legal authority to work in the United States.*

ORGANIC CHEMISTRY FACULTY POSITIONS
University of Montana

The Department of Chemistry at the University of Montana (UM) invites applications for the position as Director, the Shafizadeh Rocky Mountain Center for Wood and Carbohydrate Chemistry at the **ASSOCIATE or FULL PROFESSOR** level. The Shafizadeh Center has a tradition of research oriented toward industrial and environmentally friendly uses of carbohydrates. Applicants must have a strong background in organic carbohydrate chemistry or a related field and be able to teach undergraduate and graduate organic chemistry courses. The successful candidate is expected to have a dynamic externally funded research program and to have demonstrated excellence in teaching. The Shafizadeh Center laboratories are outfitted with modern instrumentation that includes gas chromatography/mass spectometry, high performance liquid chromatography, ion chromatography, gel permeation chromatography, differential scanning calorimetry, and computer controlled reaction equipment. Applicants should send curriculum vitae including a list of publications to: **Bruce E. Bowler, Chair, Shafizadeh Search, Department of Chemistry, University of Montana, Missoula, MT 59812. E-mail: bruce.bowler@umontana.edu.** Review of applications will commence on November 1, 2007.

Tenure-track position in organic chemistry, Department of Chemistry, the University of Montana. The Department of Chemistry invites applications at the level of **ASSISTANT PROFESSOR** in the area of organic chemistry. The development of externally funded research programs, making contributions to lower-division organic chemistry teaching and the development of upper division and graduate courses in organic chemistry are required. A Ph.D. in chemistry or a related field, postdoctoral experience in organic chemistry and a strong potential for teaching excellence is necessary. Applications, including complete curriculum vitae, a full description of research plans, and a statement of teaching philosophy should be sent to: **Nigel D. Priestley, Chair, Organic Chemistry Search Committee, Department of Chemistry, University of Montana, Missoula, MT 59812-1656. E-mail: nigel.priestley@umontana.edu.** Applicants should arrange for three letters of recommendation to be sent to the same address. Information about our Department may be accessed from our **website: http://www.umt.edu/chemistry.** The review of applications will start on November 1, 2007, and continue until the position is filled. *UM is an Affirmative Action/Equal Opportunity Employer/ADA and is a recipient of an NSF ADVANCE PACE award focused on women in science. UM encourages applications from minorities, Vietnam era veterans, and women.*

ASSISTANT/ASSOCIATE PROFESSOR of PHARMACOLOGY
University of Southern Nevada
College of Pharmacy

The University of Southern Nevada, Henderson, Nevada campus, is currently seeking applicants for a full-time (12-month) faculty position in the area of pharmacology. Responsibilities include teaching, mentoring students, providing University and community services, and participating in scholarly endeavors.

Minimum requirements include a Ph.D. in pharmacology. Postdoctoral experience is preferred; however, recent Ph.D. graduates are welcome to apply. Successful candidates should have excellent communication skills and a desire to teach in a creative and nontraditional setting. Evidence of research and other forms of intellectual initiatives are required. Salary and rank will be commensurate with qualifications and experience.

Applicants should submit a letter of intent, curriculum vitae, educational philosophy statement, and three references to: **Erik C. Jorvig, Ph.D., Faculty Recruitment Committee, University of Southern Nevada College of Pharmacy, 11 Sunset Way, Henderson, NV 89014. E-mail: ejorvig@usn.edu.** *An Affirmative Action/Equal Opportunity Employer.*

UNIVERSITY OF MICHIGAN

SCHOLARS PROGRAMS

BIOLOGICAL SCIENCES SCHOLARS PROGRAM
For Junior, Tenure-Track Faculty

The University of Michigan announces recruitment for the Biological Sciences Scholars Program (BSSP) to continue to enhance its investigational strengths in the life sciences research programs.

Now entering its 11th year, this Program has led to the recruitment of outstanding young scientists in the areas of genetics, microbiology, immunology, virology, structural biology, pharmacology, biocheistry, molecular pharmacology, stem cell biology, physiology, cell and developmental biology, and the neuosciences. The Program seeks individuals with PhD, MD, or MD/PhD degrees, at least two years of postdoccoral research experience, and evidence of superlative scientific accomplishment and scholarly promise. Successful candidates will be expected to establish a vigorous, externally-funded research program, and to become leaders in departmental and program activities, including teaching at the medical, graduate, and/or undergraduate levels. Primary college and department affiliation will be determined by the applicant's qualifications and by relevance of the applicant's research program to departmental initiatives and focus. All faculty recruited via the BSSP will be appointed at the Assistant Professor level.

APPLICATION INSTRUCTIONS: Please apply to the Scholars Programs through the BSSP web site at: (http://www.med.umich.edu/medschool/orgs/bssp). A curriculum vitae (including bibliography), a three-page research plan, an NIH biosketch, and three original letters of support should all be submitted through the BSSP web site. More information about the Scholars Programs, instructions for applicants and those submitting letters of recommendation, and how to contact us is located on the BSSP web site: (http://www.med.umich.edu/medschool/orgs/bssp). The final deadline for applications is Friday, October 19, 2007, 5:00 pm EDT.

The University of Michigan is an Affirmative Action/Equal Opportunity Employer.

University of Central Florida

Faculty Positions in Microbiology

The Burnett School of Biomedical Sciences seeks outstanding microbiologists utilizing genetic, cellular, molecular or biochemical approaches. Successful applicants will be expected to establish a well funded research program, and contribute to teaching at the undergraduate and graduate levels. Faculty at any rank will be considered. Exceptional candidates can be considered for Provost's Research Excellence Professorships. Competitive salaries, startup funds, laboratories and access to shared core instrumentation will be provided. BSL3 laboratories and animal facilities will be available. The University of Central Florida has over 48,000 students and an outstanding technology-based infrastructure. It is located in Orlando, a dynamic and progressive metropolitan region, a major player in high-tech industry, adjacent to a top ranked research park and a great place to live and work.

Review of candidates will begin on **November 15, 2007**. Please send a curriculum vitae, a two page summary of research plans and the names and contact information of three or more referees to: **Chair, Micro Search (biomed@mail.ucf.edu) 4000 Central Florida Blvd., HPAII, 335, University of Central Florida, Orlando, FL 32816-2360**.

The University of Central Florida is an Equal Opportunity, Equal Access, and Affirmative Action Employer. As a member of the Florida State University System, all application materials and selection procedures are available for public review.

University of Maryland, College Park
Chair, Department of Cell Biology and Molecular Genetics

We seek a distinguished senior scientist with a vigorous research program and the broad vision, experience, and energy to lead a period of major growth and expansion of the Department of Cell Biology and Molecular Genetics (CBMG). The expansion will include the recruitment of new senior and junior faculty and the establishment of new facilities as part of an ambitious campus drive for enhancement in the life sciences. CBMG is a vibrant, interactive and cohesive department, with research strengths in microbiology, immunology, plant biology, molecular genetics, genomics, cell and developmental biology and virology. The CBMG faculty includes prominent scientists in their respective fields with outstanding records in research, teaching and service. The research programs of the future chair and new faculty appointees will be located in spacious new laboratory facilities in the recently opened Bioscience Research Building. The successful applicant will also share a leadership role in the development of one or more of the ongoing CBMG and College of Chemical and Life Sciences initiatives in comparative and functional genomics, signal transduction, gene expression, plant biology, and host-pathogen interactions. For more information about the department, the college, and the university, visit our web site at **www.cbmg.umd.edu**.

Applicants should apply electronically by emailing an application letter with the following attachments in PDF format: (1) curriculum vitae, (2) statement of research interests, (3) statement of academic vision and administrative experience, and (4) names and addresses of at least four references to **CLFS-CBMG_Chair@umd.edu**. Review of credentials is ongoing and will continue until the position is filled.

The University of Maryland, College Park is the flagship campus of the University System of Maryland and one of the most rapidly advancing public research universities in the country. Close proximity to Washington, Baltimore, and the Maryland Biotechnology Corridor facilitates interactions with an extraordinary range of major research institutions, including the NIH, FDA, Smithsonian Institution, and USDA.

The University of Maryland is an Equal Opportunity Affirmative Action Employer. Minorities and women are encouraged to apply.

UNIVERSITY OF MARYLAND

FACULTY POSITIONS

ECOLOGY
Loyola Marymount University

The Department of Biology seeks a broadly trained **ECOLOGIST** for a tenure-track position at the rank of **ASSISTANT PROFESSOR.** The successful candidate will possess a Ph.D. in biology, botany, zoology or equivalent, plus strong interest and capability in field-oriented research and teaching. Teaching responsibilities include lower-division courses, upper-division courses in ecology and in the candidate's area of specialization, and a senior-level seminar.

The successful candidate must develop an active research program which involves undergraduates. University and Department service and scholarly publication are required.

Loyola Marymount University, established in 1911, is the only Jesuit University in southern California. Over 6,000 students are enrolled in the Colleges of Liberal Arts, Business Administration, Science and Engineering, Communication and Fine Arts, the Schools of Education and Film and Television, and the Law School. The campus is situated on a bluff overlooking the Pacific Ocean and Los Angeles' west side, and is from minutes to half a day's travel to beach, dune, mountain, chaparral, desert, wetlands, marine, and California Channel Islands communities. The Department also maintains a biological station in Baja California, Mexico.

The Biology Department has 12 faculty dedicated to undergraduate teaching and research and welcomes candidates who desire to work in such an environment. Faculty are also engaged in interdisciplinary efforts in several areas, including biomathematics and environmental studies of the nearby Ballona Wetlands; the Ecologist's participation would be welcomed. The Department is housed in a renovated science building which includes facilities equipped for supporting field and laboratory research.

Interested individuals should send letter of application, curriculum vitae, research and teaching statements, graduate transcripts, selected publications, and three letters of reference by November 1, 2007, to: **Ecology Search Committee, Department of Biology, Loyola Marymount University, 1 LMU Drive, M.S. 8220, Los Angeles, CA 90045-2659.** For additional information, contact **Dr. Martin G. Ramirez, telephone: 310- 338-5120. (Visit website: http://www.lmu.edu for more information.)**

Loyola Marymount, a comprehensive university in the mainstream of American Catholic higher education, seeks professionally outstanding applicants who value its mission and share its commitment to academic excellence, the education of the whole person, and the building of a just society. LMU is an equal opportunity institution actively working to promote an intercultural learning community. Women and minorities are encouraged to apply.

FACULTY POSITION at the UNIVERSITY of PUERTO RICO

The Department of Biology of the University of Puerto Rico at Rio Piedras **(website: http://biology.uprrp.edu)** invites applications for a tenure-track position in systematics/biodiversity/macroecology. The candidate is expected to curate and improve the zoological collection and to implement museum database programs (research interest in invertebrates and strong collections management and curatorial background are desirable). Applicants must hold a Ph.D. or equivalent and have postdoctoral experience. The candidate is expected to develop an active research program and to teach at the graduate and undergraduate levels. Interested persons should send resume, a statement of current and future research and teaching goals, representative publications and three letters of reference to: **Dr. James Ackerman, P.O. Box 23360, UPR Station, San Juan, PR 00931-3360** or **e-mail: ackerman.upr@gmail.com.** Applications will be reviewed from October 1, 2007, until the position is filled. *University of Puerto Rico is an Equal Opportunity Employer.*

THE UNIVERSITY of TENNESSEE HEALTH SCIENCE CENTER

TENURE-TRACK FACULTY POSITIONS
The Department of Molecular Sciences
College of Medicine, University of Tennessee Health Science Center, Memphis

The University of Tennessee Health Science Center Department of Molecular Sciences seeks two full-time tenure-track faculty at the **JUNIOR or SENIOR** level with basic or translational research experience investigating aspects of molecular pathogenesis of infections, vaccine development, emerging infections and select agents, genetics of host-pathogen interactions, and antimicrobial resistance. We seek to expand our strong interdisciplinary group of basic and clinical scientists as we integrate additional research programs into our campuswide clinical and translational research programs and new Regional Biocontainment Laboratory. Core campus resources include extensive mouse genomics and informatics, Molecular Resource Center, good manufacturing practice facilities, and BSL-3 suites for high throughput screening, small animal imaging and microscopy. Adjunct appointment in the appropriate clinical departments and collaboration with the V.A. Hospital and St. Jude Children's Research Hospital are encouraged. Applicants must have a Ph.D., M.D., or D.V.M. with an established reputation in one of the above areas of research.

Successful candidates will be responsible for developing and maintaining an extramurally funded, independent research program and contribute to graduate and professional student teaching. Interested applicants should send a letter of interest, brief description of research accomplishments, short summary of future research plans, and curriculum vitae, and arrange to have three letters of reference sent to: **Dr. Lorraine Albritton, Chair of the Search Committee, Department of Molecular Sciences, The University of Tennessee Health Science Center, 858 Madison Avenue, Memphis, TN 38163,** or **e-mail: lalbritt@utmem.edu.** Review of applications will begin immediately and continue until all positions are filled. For additional information, see **website: http://www.utmem.edu/molecular_sciences.** *The University of Tennessee is an Equal Opportunity/Affirmative Action/Title VI/Title IX/Section 504/ADA/ADEA Employer. Women and minorities are encouraged to apply.*

FACULTY POSITION in PHYSIOLOGY and NEUROBIOLOGY

The Department of Physiology and Neurobiology at the University of Connecticut, Storrs, invites applications for a tenure-track faculty position available in fall 2008, at the **ASSISTANT or ASSOCIATE PROFESSOR** level. The successful candidate will be expected to maintain an independent and vigorous research program and participate in the Department's graduate and undergraduate teaching. We encourage applications from individuals studying fundamental physiological or neural processes at the molecular, cellular, or systems level. Special consideration will be given to those emphasizing membrane biology. Applicants must possess a Ph.D. and have completed at least two years of postdoctoral training. Candidates for Associate Professor are expected to have a currently funded and active research program. Review of candidates will begin on October 1, 2007, and the search will continue until the position is filled. Send curriculum vitae, a brief summary of current research with a statement of research directions, a statement of teaching interests, and the names of at least three references to: **Chair, PNB Search Committee, University of Connecticut, Department of Physiology and Neurobiology, Box U-3156, 75 North Eagleville Road, Storrs, CT 06269-3156. Website: http://www.pnb.uconn.edu.**

FISH PHYSIOLOGY/AQUACULTURE

The Southern Illinois University Carbondale Department of Zoology invites applications for a 12-month, tenure-track **ASSISTANT PROFESSOR** position in fish physiology/aquaculture with 75 percent research in the Fisheries and Illinois Aquaculture Center and 25 percent teaching in zoology. The Department seeks a physiologically oriented **AQUACULTURIST** with experience with finfish of regional importance, experience/capability in environmental physiology of fish, and who has potential/motivation to establish a record of research and related scholarly activities to accelerate a prominent personal research program within a nationally recognized fisheries center. The successful candidate will complement existing strengths in aquaculture, fish and aquatic ecology, fish genetics, fisheries management, aquatic toxicology, and ichthyology. Applicants should have demonstrated skills in experimental design and statistical analyses. Modern research facilities and startup funds are available.

The successful candidate will be expected to develop an externally funded research program, supervise M.S. and Ph.D. students, and teach environmental physiology of fish and comparative endocrinology or another undergraduate and/or graduate course in his/her specialty.

Candidates must have a Ph.D. in an appropriate field with a record of peer-reviewed publications and scholarly accomplishments commensurate with experience, and demonstrated grant success or strong evidence of funding potential. Preference will be given to applicants with postdoctoral teaching and research experience and membership in the American Fisheries Society and/or the World Aquaculture Society.

Applicants should send curriculum vitae, statement of teaching and research interests and plans, copies of transcripts from all institutions attended, representative reprints, and have four letters of reference sent to: **Dr. Christopher C. Kohler, Fisheries and Illinois Aquaculture Center, Mail code 6511, 1125 Lincoln Drive, Southern Illinois University Carbondale, Carbondale, IL 62901.** Review of applications will begin on 15 October 2007 and continue until the position is filled. Information about the Department, University, and Center can be found at **websites: http://www.science.siu.edu/zoology, http://fisheries.siu.edu.** E-mail inquiries (not applications) should be directed to the **Search Committee Chair (e-mail: ckohler@siu.edu).**

SIUC is an Affirmative Action/Equal Opportunity Employer that strives to enhance its ability to develop a diverse faculty and staff and to increase its potential to serve a diverse student population. All applicants are welcomed and encouraged and will receive consideration.

FACULTY POSITIONS in BIOLOGY
The Scripps Research Institute (TSRI)
La Jolla, California

As part of a new research initiative at the Scripps Research Institute, we are seeking outstanding applicants for multiple tenure-track/tenured faculty positions at the **ASSISTANT OR ASSOCIATE PROFESSOR** levels. Applicants in all areas of biology will be considered.

Applicants should conduct innovative basic research that has the potential to contribute to translational medical research, and have demonstrated potential to be a leader in their field.

Applicants should send their curriculum vitae, a brief statement of research interests, and three letters of reference by November 1, 2007, to:

The Scripps Research Insititute Faculty Search Committee
c/o Marisol Chacon
The Scripps Research Institute
10550 N. Torrey Pines Road, ICND222
La Jolla, CA 92037

THE COMMONWEALTH MEDICAL COLLEGE*

Founding Faculty: Master Teachers and Researchers
Assistant Professors – Associate Professors – Full Professors

The Commonwealth Medical College, a new independent medical school in Pennsylvania is searching for a founding basic science faculty who want to practice state of the art teaching and engage in research in a collaborative setting. This is a chance for faculty to help shape the future of a new, innovative model of medical education. The Commonwealth Medical College will train in a community based, distributive model working with clinical faculty throughout north central and northeastern Pennsylvania, linked by state of the art technology. We are in the accreditation process with LCME and the Pennsylvania Department of Education and hope to accept our first class in 2009. We are funded by state dollars and a generous grant from Blue Cross of Northeastern Pennsylvania. The school enjoys tremendous regional support for its mission of education, research and service and has developed relationships with outstanding local colleges, universities, hospitals and physicians to create a new model of medical education.

We are looking for exceptional faculty in pathology and all basic science areas – biochemistry, physiology, microbiology, and anatomy, who are passionate about teaching and research, interested in mentoring students, and want to participate in an interdisciplinary, collaborative model. We are also seeking faculty who want to build something new, who are comfortable with technology and new teaching methods.

We are interested in scientists who want to grow and develop their research in a new academic model. Our initial interests are in genomics, pharmacogenomics, pharmokinetics (PK) and pharmacodynamics (PD) that are relevant to cancer and epidemiologically important infections and diseases. We are also interested in developing a clinical research center model that would involve community physicians and hospitals and conducting population based studies related to the health needs of the area. Cancer, diabetes, and heart disease are the leading issues of concern, but other areas of expertise are also welcomed.

This is a wonderful opportunity to create something innovative and important and have a significant impact on the future of a new medical school. Unlimited opportunities for growth, both professionally and personally, exist within this collaborative environment. We will be developing curriculum, as well as new facilities, with faculty input.

Please submit your curriculum vitae to: Robert M. D'Alessandri, MD, Dean, The Commonwealth Medical College, 150 North Washington Avenue, Scranton, PA 18503 or electronically to RMD@nepamedc.org.

thecommonwealthmedical.com | The link to the Dean's blog is newmedicalschool.blogspot.com

**This school is proposed and in development phase. Not yet granted degree granting authority from the Pennsylvania Department of Education.*

COLUMBIA UNIVERSITY MEDICAL CENTER
Faculty Position
Department of Genetics and Development

The Department of Genetics and Development at Columbia University Medical Center is expanding its faculty and seeks outstanding applicants with the ability to develop an independent research program for a tenure-track position at the Assistant Professor level. In special circumstances, applicants at the Associate Professor level may also be considered. Applicant's research program should rely on genetic and molecular approaches to study, in vertebrates or invertebrates, any questions relevant to human development, physiology, and the bases of degenerative diseases. Our department spans a broad range of interests including developmental biology, physiology, DNA recombination, cancer genetics, and human genetics. Applicants should include a curriculum vita and a summary of current and proposed research programs and arrange for three letters of reference to be sent. Completed applications and letters of reference should be sent electronically to:

Genetics Search Committee
Attn: Celia Morales
cr2020@columbia.edu

Consideration for completed applications will begin October 12, 2007.

Columbia University is an equal opportunity/ affirmative action employer. Women and minorities are encouraged to apply.

TEXAS A&M
HEALTH SCIENCE CENTER
COLLEGE OF MEDICINE

Tenure-track faculty positions in Systems Biology and Translational Medicine

State of Texas funded tenure-track positions at the Assistant and Associate Professor levels are available in 5 areas:

- Systems biology, analysis of gene and signaling networks, bioinformatics and computational biology, genomics, proteomics.
- Regenerative medicine, developmental biology, stem cell biology, tissue engineering, organogenesis.
- Imaging at molecular, cellular and organismal levels.
- Gene therapy, targeted delivery of oligonucleotides, proteins or pharmaceutical agents to specific cells, nanotechnology.
- Molecular basis of ion channel function, patch clamping, optical recording of ion channel activity, mutant channel proteins.

New faculty will instruct medical and/or graduate students and will be active in predoctoral and postdoctoral training. Competitive salary and generous start-up packages are available.

The Department of Systems Biology and Translational Medicine in the College of Medicine consists of 15 faculty members and embraces the convergence of human biology and the quantitative sciences, including engineering, mathematics, physics and computer science. A primary focus of the department is on the cardiovascular system, from the molecular to organismal levels of organization. However, individuals with expertise in other organ systems or cell types are strongly encouraged to apply. Departmental core facilities include: microarray, imaging (confocal and atomic force), and bioinformatics/computational biology. Campus cores include: proteomics, cell sorting and analysis, laser capture microdissection and whole animal imaging. Interactions with clinical researchers are possible through Scott & White Clinic and Central Texas Veterans Health Center, the major teaching hospitals of the Texas A&M Health Science Center. The department participates in the multidisciplinary Medical Sciences graduate program and is active in postdoctoral training. The College of Medicine is entering a rapid growth phase due to expansion of the medical class, and the department expects to recruit a substantial number of new faculty members in the next 3 years.

Send CV, statement of research, training and teaching goals, and a list of at least 3 references to **granger@tamu.edu** or **Harris J. Granger, PhD, Department of Systems Biology & Translational Medicine, College of Medicine, Texas A&M Health Science Center, 702 SW HK Dodgen Loop, Temple, Texas 76504-7105.**

FACULTY POSITIONS

PARASITOLOGY

Southern Illinois University Carbondale (SIUC), the College of Science seeks an outstanding Scientist in the general area of parasitology to complete a research cluster in pathogenesis/parasitology/epidemiology as an ongoing part of SIUC's commitment to enhance interdisciplinary research (**website: http://news.siu.edu/s150/**). Southern Illinois University Carbondale is a large, public, comprehensive research-intensive university situated in a pleasant small-town setting southeast of St. Louis.

The Department of Zoology at SIUC invites applications for a tenure-track position as an **ASSISTANT PROFESSOR** with a start date of August 16, 2008. Applicants must hold a Ph.D. or other appropriate doctoral degree and have a record of relevant postdoctoral research training by the time of appointment. The applicant must also have an externally funded research program or the potential for developing one, as well as a significant record of peer-reviewed publications.

The successful candidate will enhance and complement existing programmatic strengths in the areas of ecology, environmental biology, conservation, biodiversity, and evolutionary biology with a basic research program in some aspect of parasite biology such as host-pathogen interactions or co-evolution, host defense mechanisms, host specificity, epidemiology, biogeography, population dynamics, responses to environmental factors, or development of methods and agents to combat parasites. Modern research facilities and startup funds are available. The successful applicant is expected to teach an introductory parasitology course, help teach animal diversity, and a graduate-level course dependent upon the individual's expertise and program needs. The Department of Zoology, with a faculty of 25, offers B.S., M.S., and Ph.D. degrees (**website: http://www.science.siu.edu/zoology/**).

Applications: Review of applications will begin October 15, 2007, and continue until the positions are filled. Applicants should submit curriculum vitae, a statement of teaching and research interests, and the names and addresses of at least three references to: **Parasitology Search Committee Chair, Department of Zoology, Mailcode 6501, 1125 Lincoln Drive, Southern Illinois University Carbondale, Carbondale, IL 62901. E-mail: zoology@zoology.siu.edu.**

SIUC is an Affirmative Action/Equal Opportunity Employer that strives to develop a diverse faculty and staff and to increase its potential to serve a diverse student population. All applications are encouraged and will receive consideration.

BIOLOGIST/BIOINFORMATICS/PROTEIN STRUCTURE

The Department of Biological Sciences at Marquette University has a tenure-track **ASSISTANT PROFESSOR** position available August 16, 2008. Applicants must have a Ph.D. with postdoctoral experience. The successful candidate is expected to develop an extramurally funded research program that will complement existing areas of research within the Department (**website: http://biology.marquette.edu**). Preference will be given to applicants who can also provide expertise in bioinformatics, genomics or protein structure that enhances ongoing programs campus-wide. Teaching responsibilities include an introductory biology course for undergraduate majors and a graduate course in the candidate's area of expertise each year. Review of applications until the position is filled. Candidates should apply online at **website: http://careers.marquette.edu/applicants/Central?quickFind=51073** Application process requires curriculum vitae and statement of research and teaching interests. Three reference letters are to be sent to: **Dr. Robert Fitts, Chair, Department of Biological Sciences, Marquette University, WLS 112, P.O. Box 1881, Milwaukee, WI 53201-1881.**

FACULTY POSITIONS

THE UNIVERSITY of WISCONSIN MADISON

FACULTY POSITION
Neuroplasticity
University of Wisconsin, Madison

The Center for Neuroscience at the University of Wisconsin, Madison, is seeking a **NEUROSCIENTIST** interested in developing an interdisciplinary research program dedicated to neuroplasticity with special emphasis on neuropharmacology for a tenure-track **JUNIOR or SENIOR FACULTY** position. Areas of interest include, but are not limited to, pharmacology, synaptic plasticity, and molecular and cellular mechanisms of learning and memory. Research programs investigating phenomena and mechanisms of plasticity at all levels of biological organization including clinical applications will be considered. These faculty positions are part of the neuroscience initiative at the University of Wisconsin, Madison (see **website: http://www.neuroscience.wisc.edu).**

Appropriate credentials may be Ph.D. and/or M.D., or equivalent degrees, with responsibilities including research, teaching, and other activities commensurate with background and experience. The successful candidate should have a record of outstanding research achievements and the potential to develop a strong independent research program. Please submit curriculum vitae, a summary of research program goals, three to five recent publications and three letters of reference electronically to:

Thomas Sutula
Search Committee Chair
Director, Center for Neuroscience
E-mail: sutula@neurology.wisc.edu
Arnold E. Ruoho
Search Committee Co-Chair
Chair, Department of Pharmacology
E-mail: acruoho@wisc.edu

Note: Unless confidentiality is requested in writing, information regarding the names of applicants must be released upon request. Finalists cannot be guaranteed confidentiality. UW, Madison, is an Equal Opportunity/Affirmative Action Employer.

DEVELOPMENTAL BIOLOGIST

The Biology Department of Albion College announces a search for a tenure-track Developmental Biologist at the rank of **ASSISTANT PROFESSOR,** to begin in August 2008. A Ph.D. is required. College teaching experience and a demonstrated record of scholarship are preferred. The successful candidate will be expected to teach a majors course in developmental biology and develop a course in his or her area of expertise. The candidate also will share responsibilities in an introductory cell and molecular biology course. A research agenda that incorporates undergraduate students is expected. Facilities include a new, well-equipped, interdisciplinary science complex, state-of-the-art molecular biology equipment, a wide array of teaching and research-grade microscopes, and controlled-environment chambers. Albion College is a selective, liberal arts college of 1,900 students located in a diverse community of 9,000 people in south central Michigan, within an hour's drive of three major universities. See **website: http://www.albion.edu/biology/** for further information and a more comprehensive listing of instrumentation and resources. Send letter of application, statements on teaching and research interests, curriculum vitae, graduate and undergraduate transcripts, recent reprints, and three letters of reference (electronic copies not acceptable) to: **Dr. Ruth E. Schmitter, Biology Department, Albion College, Albion, MI 49224-1831.** The deadline for completed applications is October 15, 2007. *Albion College is an Equal Opportunity Employer committed to diversity as a core institutional value.*

FACULTY POSITIONS

ASSISTANT PROFESSORSHIPS in BIOLOGY
Western Washington University

The Biology Department at Western Washington University, a regional comprehensive university located between Seattle and Vancouver, British Columbia, invites applications for three tenure-track, **ASSISTANT PROFESSOR** positions, beginning September 2008. We seek individuals committed to undergraduate and M.S. education who will establish vigorous research programs that involve students.

EUKARYOTIC CELLULAR MOLECULAR BIOLOGIST: Ph.D. and postdoctoral experience in eukaryotic cellular and molecular biology required. Applicants must provide evidence of the ability to teach introductory and advanced courses in cell biology or genetics and in molecular biology techniques. We are interested in applicants with expertise in eukaryotic systems at the cellular level, who use molecular and/or genetic methods to address fundamental research questions. Review begins November 1, 2007.

ECOLOGICAL GENETICIST: Ph.D. and postdoctoral experience in genetics, ecology, or evolutionary biology required. Applicants must have training in ecological genetics and provide evidence of the ability to teach upper-level courses in general genetics and evolutionary biology. Applicants who are broadly trained with expertise in quantitative genetics and/or genomics and with strong statistical skills are of particular interest. Review begins October 22, 2007.

NEUROBIOLOGIST: Ph.D. and postdoctoral experience in neurobiology required. Applicants who can contribute a molecular and cellular approach to an emerging behavioral neurosciences program are of particular interest. The applicant must provide evidence of the ability to teach introductory animal physiology and advanced courses in neurobiology and in cell biology or genetics. Review begins November 1, 2007. See full position announcements, including all required qualifications, at **website: http://biol.wwu.edu/biology/.** To apply, submit curriculum vitae, statements of teaching and research interests, and three letters of reference. All materials should be sent to the attention of: **Dr. Jeffrey Young, Chair: Eukaryotic Cellular Molecular Biology Search Committee; Dr. Merrill Peterson, Chair: Ecological Genetics Search Committee; Dr. David Leaf, Chair: Neurobiology Search Committee; Biology Department, Western Washington University, 516 High Street, Bellingham, WA 98225-9160.** *Affirmative Action/Equal Opportunity Employer.*

TENURE-TRACK FACULTY POSITION
Biochemistry

The Department of Chemistry and Biochemistry at the University of San Diego (**website: http://www.sandiego.edu/chemistry**), an independent Catholic university, invites applications for an open-rank tenure-track position in biochemistry beginning fall 2008. The Department is housed in a new 150,000 square foot interdisciplinary science facility boasting over $3 million in new instrumentation and equipment, including 400 and 500 megahertz nuclear magnetic resonanace spectrometers. The successful candidate will have a commitment to undergraduate education; have the ability to teach a range of undergraduate level courses including biochemistry (lecture and laboratory), general chemistry, and specialized courses; and to establish a vigorous undergraduate research program. Female and minority candidates are especially encouraged to apply. Please send curriculum vitae, transcripts (undergraduate and graduate), statement of teaching philosophy, research plans, and three letters of recommendation to: **Biochemistry Search Committee, Department of Chemistry and Biochemistry, University of San Diego, 5998 Alcala Park, San Diego, CA 92110.** Applications must be received by October 15, 2007, for full consideration. *USD is an Equal Opportunity Employer.*

ASSISTANT PROFESSOR IN COMPUTATIONAL BIOLOGY #1164S

The University of California, Berkeley invites applications for a position in the area of Computational Biology at the assistant (tenure track) professor level starting July 1, 2008. The University has committed to establishing Berkeley as a premier institution for education, training and research in Computational Biology, with extensive research activities, full integration between multiple UC campuses through QB3, and relevant programs at the Lawrence Berkeley National Laboratory (LBNL) and the Joint Genome Institute (JGI). This position is associated with the Center for Computational Biology, which includes computational scientists across the full spectrum of the mathematical, physical, engineering and biological sciences, creating an exceptional environment for both research and education in this rapidly growing field. The focus of this position is on the physical sciences, and the holder of the position will have a primary appointment in an academic department appropriate to his or her interests.

Applicants should have a research focus in the broad area of Computational Biology and hold (or be about to receive) a doctoral degree or equivalent in a quantitative field. The scope of the position includes innovative approaches to major problems in computational biology using physical, chemical, or engineering principles. Specialized areas may include, but are not limited to:

- **Protein structure and function, ligand and protein design**
- **Protein complexes, molecular machines, cellular modeling**
- **Multiscale biological modeling, molecular mechanics and dynamics**

We seek individuals with demonstrated excellence in research, and the potential for excellence in teaching and leadership. Successful applicants will be expected to establish a pre-eminent research and educational program, and develop and teach courses in appropriate areas of the computational sciences.

Applicants should send a curriculum vitae, a selection of publication reprints (five or less), and a brief statement of research plans and teaching interests, highly preferred to be sent electronically, in pdf format, to the email address below. The applicant should also arrange for three letters of reference to arrive by **December 1, 2007**, to the same email address below. Please refer potential reviewers to the UC Berkeley Statement of Confidentiality found at: **http://apo.chance.berkeley.edu/evalltr.html**.

cbi@berkeley.edu (electronic/pdf submissions strongly preferred)
-or-
Chair, Computational Biology Search Committee
Center for Computational Biology,#1164S
University of California, Berkeley
304 Stanley Hall #3220
Berkeley, CA 94720-3220

All applications must be complete by **December 1, 2007** for consideration in this year's recruitment cycle.

The University of California is an Equal Opportunity/Affirmative Action Employer.

Tenure Track Faculty Position: Environmental Biologist

McDaniel College invites applications for a tenure track appointment at the Assistant Professor level in Environmental Biology, with botanical emphasis, to begin Fall, 2008. Responsibilities include courses in Ecology, Botany and Population Biology, as well as participation in freshman courses and senior research projects. Applicants must be willing to participate in the College's First Year Seminar and other general education programs. PhD strongly preferred; ABD required.

Interested applicants should send a letter of application, *curriculum vitae*, three letters of reference, a statement of teaching philosophy, and a statement about research to be done with students to: **Dr. Wilbur Long, Biology Department, McDaniel College, 2 College Hill, Westminster, MD 21157-4390**. Electronic applications should be addressed to **wlong@mcdaniel.edu**. Application review will begin on **October 22, 2007**.

One of forty colleges and universities nationwide known for its success at changing the lives of its students, McDaniel College is a selective liberal arts college located in central Maryland, an hour's drive from Baltimore and Washington, DC. Its primary commitment is to outstanding teaching and to fostering critical and creative thinking and humane and responsible action.

McDaniel College, an AA/EEO and an award-winning ADA Employer, welcomes applications from women and men of diverse racial/ethnic backgrounds.

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Faculty Positions in Physics of Biological Systems
at Ecole Polytechnique Fédérale de Lausanne (EPFL)

The School of Basic Sciences at EPFL anticipates making several appointments at the level of tenure track Assistant Professor in the broad field of physics of biological systems. The open faculty positions are offered in an environment of both theoretical and experimental research, at the interface between physical and biological sciences. The appointed Professors will enjoy close contacts with the School of Life Sciences of EPFL, the School of Biology and Medicine of the University of Lausanne, and the University Hospital of the Canton de Vaud (CHUV).

Outstanding candidates with recognized accomplishments investigating the structure, dynamics and function of biological systems from the molecular to the cellular levels are particularly encouraged to apply. Proposed research activities covering advanced imaging techniques are also of interest. Existing research facilities are strong in bio-imaging and electron-microscopy, including access to the Swiss light source for synchrotron radiation.

Successful candidates are expected to initiate independent, creative research programs and be committed to excellence in undergraduate and graduate teaching. We offer internationally competitive salaries, start-up resources and benefits.

Applications including curriculum vitae, publication list, concise statement of research and teaching interests as well as the names and addresses (including email) of at least five references should be submitted in PDF format via the website http://sb.epfl.ch/physsearch **by November 1, 2007.** Inquiries may be directed to **Prof. Rolf Gruetter** (rg_physbio@epfl.ch).

For additional information on EPFL, please consult: http://www.epfl.ch, http://sb.epfl.ch, http://sv.epfl.ch

EPFL is committed to balance genders within its faculty and most strongly encourages qualified women to apply.

FACULTY POSITIONS

CHAIR

The Department of Physics and Astronomy at the University of Waterloo, Canada, invites nominations and applications for the position of **CHAIR OF THE DEPARTMENT.** Candidates are expected to have a distinguished record of teaching, research and demonstrated ability in leadership and administration. They should also be eligible for a faculty position, normally at the level of **FULL PROFESSOR.** The successful candidate will set the academic tone for the Department, be responsible for the relationship between the Department and the broader academic community, and play a leading role in the academic planning and management process within the Faculty of Science.

The Department has more than 50 full-time members of faculty and staff, 110 graduate students and postdoctoral fellows and 200 honours undergraduate physics and astronomy students. Undergraduate studies are available in both a Cooperative Education and Regular format. The Department has close ties to both the Institute for Quantum Computing and the Perimeter Institute. The Department is research active and attracts outstanding Canadian and international applicants to its graduate program.

The University of Waterloo is located in the attractive two-university community of Kitchener-Waterloo (population 300,000) in southwestern Ontario, about one hour west of Toronto.

Applications and nominations should include a detailed resume, the names and contact information for three individuals willing to provide references, and a statement of capabilities and qualification. For full consideration, applications should be received prior to October 15, 2007. Send applications or nominations to:

Professor Terry McMahon, Dean
Faculty of Science
University of Waterloo
200 University Avenue,
West Waterloo, Ontario
Canada, N2L 3G1

Telphone: 519-888-4591; fax: 519-746-2543; e-mail: lweber@uwaterloo.ca.

All qualified candidates are encouraged to apply; however Canadian citizens and permanent residents will be given priority. The University of Waterloo encourages applications from all qualified individuals, including women, members of visible minorities, native people and persons with disabilities.

ASSISTANT PROFESSOR in BIOCHEMISTRY

The Chemistry Department of the U.S. Naval Academy invites applications for one or more tenure-track positions in biochemistry at the **ASSISTANT PROFESSOR** level to begin August 2008. The Department consists of 39 full-time faculty members including five biology/biochemistry faculty, and occupies over 52,000 square feet of newly renovated office, classroom, and laboratory space equipped with a wide array of modern instrumentation and computer facilities. Approximately 30 students per year graduate with American Chemical Society-certified chemistry degrees, and planning is underway for a biochemistry track. The successful applicant must be strongly committed to teaching at the undergraduate level and will be expected to help teach general chemistry and biochemistry courses on a rotating basis. In addition, the candidate of choice will be expected to develop and maintain a vigorous research program which includes supervision of undergraduate researchers. Candidates should send curriculum vitae, statement of teaching philosophy, concise description of research/scholarly interests and arrange for three letters of recommendation (at least one of which addresses teaching) to be sent by October 22, 2007, to: **Search Committee, Chemistry Department, U.S. Naval Academy, 572 Holloway Road, Annapolis, MD 21402-5026.** *The U.S. Naval Academy is committed to identifying minority persons and women with the appropriate qualifications and is an Equal Opportunity/Affirmative Action Employer. This agency provides reasonable accommodations to applicants with disabilities.*

Washington University in St. Louis
SCHOOL OF MEDICINE

FACULTY POSITION in DEPARTMENT of CELL BIOLOGY and PHYSIOLOGY
Molecular Oncology Program

The Department of Cell Biology and Physiology at Washington University School of Medicine invites applications for a tenure-track appointment at the rank of **ASSISTANT PROFESSOR.** The successful candidate will join the Molecular Oncology Program, a joint program between the Departments of Cell Biology and Internal Medicine at Washington University School of Medicine. The Molecular Oncology Program is comprised of a vibrant group of interactive investigators studying cell cycle control, checkpoint control, cell death, G-protein signaling, telomere biology, HIV pathogenesis, metastasis, oncogenes, and tumor suppressors. Outstanding individuals investigating fundamental problems in molecular oncology are encouraged to apply. Candidates must demonstrate the ability to develop an independent research program and a commitment to excellence in graduate education. Applicants must have a Ph.D. and/or M.D. and postdoctoral experience. Please send curriculum vitae, a summary of current and proposed research programs, and arrange for three letters of recommendation to be sent to:

Drs. Helen Piwnica-Worms and Kendall J. Blumer, Co-Chairs
Cell Biology and Physiology Search Committee
Washington University School of Medicine
660 South Euclid Avenue - Campus Box 8228
St. Louis, MO 63110
E-mail: facultysearch@cellbiology.wustl.edu

Applications should be received by February 1, 2008. *Washington University is committed to increasing representation of women and members of minority groups on its faculty and particularly encourages applications from such candidates.*

BIOCHEMISTRY POSITIONS

Washington University in St. Louis seeks to fill two positions to begin in the fall 2008 in any area of biochemistry. One position will be located in the Department of Chemistry in the School of Arts and Sciences. The other position will be located in the Department of Biochemistry and Biophysics at the School of Medicine. A successful candidate will hold their primary appointment in the Department in which they are located. In addition, each position holds the potential for a joint appointment in the second Department. The development and maintenance of an outstanding research program and the teaching of both core and advanced biochemistry courses are required. Applications should consist of curriculum vitae and a concise research proposal or proposals. These documents are to be submitted in electronic form as PDF (portable document format) files to **e-mail: search@wuchem.wustl.edu** with the subject line Biochemistry Faculty Search. Applicants should also arrange for three letters of reference to be sent to **e-mail: search@wuchem.wustl.edu,** with signed originals sent to:

Biochemistry Faculty Search Committee
Department of Chemistry
Campus Box 1134
Washington University
One Brookings Drive
St. Louis, MO 63130-4899
Fax: 314-935-4481

Completed applications for the position must be received by 15 October 2007, to ensure inclusion in the initial review. However, applications received later will be accepted and reviewed until a candidate has been hired or the search discontinued. While an emphasis will be place on hiring at the **JUNIOR FACULTY** level, truly exceptional applications at all levels will be considered. *Washington University is an Equal Opportunity, Affirmative Action Employer. Individuals from underrepresented groups are especially encouraged to apply.*

TENURE-TRACK FACULTY POSITION
Endocrine Division/Center for Molecular Medicine and Genetics
Wayne State University School of Medicine

A tenure-track position for an outstanding Physician-Scientist (M.D. or M.D.-Ph.D. degrees) at the **ASSISTANT, ASSOCIATE, or FULL PROFESSOR** level is available as a joint appointment between the Endocrine Division of the Department of Internal Medicine and the Center for Molecular Medicine and Genetics **(website: http://www.genetics.wayne.edu).** The appointee would be housed in the laboratories of the Center, which recently underwent a $20 million renovation of its laboratory and core research facilities. The candidate would join an active faculty conducting basic and translational research. An attractive startup package is available, which includes the proceeds from a $1 million (Brasza family) endowment intended to support diabetes research. The Division of Endocrinology serves inpatient and outpatient endocrine/diabetes patients at the Detroit Medical Center hospitals, which are over 1,000-bed facilities. There are ample opportunities for both basic and clinical research in diabetes. The scientific environment includes several basic scientists with active NIH-funded research in beta cell biology, insulin actions, mitochondrial signaling, adipokines, and diabetes complications. The Endocrine Division has an Accreditation Council for Graduate Medical Education-approved fellowship program. We are recruiting a candidate who has areas of ongoing diabetes research in translational genetics or genomics, including inborn errors of metabolism, mitochondrial disorders, or treatment of genetic disorders. There are extensive opportunities for collaboration and excellent opportunities to develop translational research with industry, government, and other academic institutions. Wayne State University is Michigan's only research university located in an urban setting. Applications will be reviewed upon receipt and review continued until the position has been filled.

Applications should include a letter of application, curriculum vitae, and the names and addresses of at least three references and be sent to: **Ms. Mary Anne Housey, Center for Molecular Medicine and Genetics, Wayne State University School of Medicine, Rm. 3127 Scott Hall, 540 E. Canfield Avenue, Detroit, MI 48201 or by e-mail: mhousey@genetics.wayne.edu.**

WSU, an Equal Opportunity/Affirmative Action Employer.

VIROLOGIST

The Division of Biological Sciences at the University of Montana is seeking a Virologist working in infectious disease who complements current research areas and can participate in teaching virology at the graduate and undergraduate levels.

This tenure-track position is at the **ASSISTANT or ASSOCIATE** level, depending on qualifications. The ideal applicant will have postdoctoral research experience, evidence of teaching excellence, an established record of research productivity, and demonstrated success or potential to secure research funding.

The new hire will join a diverse group of active faculty in the graduate programs in integrative microbiology and biochemistry, who enjoy collegial interactions with faculty in a variety of other graduate programs (see **websites: http://dbs.umt.edu/** and **http://virologist.dbs.umt.edu).**

Applicants should send curriculum vitae, statements of research and teaching interests, and names of three references to: **Chair, Virologist Search Committee, Division of Biological Sciences, University of Montana, 32 Campus Drive, Missoula, MT 59812,** or submit electronically to **e-mail: virology.search@mso.umt.edu.** Review of materials will begin October 15, 2007. The Division is interested in hiring a candidate who will enhance the ethnic and gender diversity of its faculty. *UM is an Affirmative Action/Equal Opportunity Employer/ADA/Veterans Preference Employer and the recipient of an active NSF PACE award. This material is available in an alternative format upon request.*

DUKE NUS
GRADUATE MEDICAL SCHOOL SINGAPORE

Faculty Positions
Cancer and Stem Cell Biology

The Duke-NUS Graduate Medical School Singapore (Duke-NUS GMS), a global partnership between the Duke University and the National University of Singapore, is recruiting internationally. We seek creative scientists who are focusing on discovery biology and/or translational medicine in the field of **Cancer and Stem Cell Biology.**

Applicants for all ranks should have a PhD, MD, or equivalent and a record demonstrating outstanding promise. Special opportunities exist for research involving cancer stem cells, advanced imaging, and translational studies both in non-human primates and in collaboration with world-class clinical services, including Singapore's National Cancer Centre and General Hospital. Successful applicants will join investigators already affiliated with Duke-NUS GMS (see www.gms.edu.sg). Faculty positions include full salary, generous start-up, and research funding of up to S$500K/p.a., assuring a stable base of support that can be supplemented by competitive grant awards, which are expanding rapidly in Singapore.

Interested candidates should send a cover letter, curriculum vitae, a summary of research accomplishments and future plans, and arrange for three letters of reference to be forwarded (Assistant Professor candidates), no later than 9 November 2007, to:

David Virshup, Director
Program in Cancer and Stem Cell Biology
Duke-NUS Graduate Medical School Singapore
2 Jalan Bukit Merah, Singapore 169547
email to: CSB.recruit@gms.edu.sg

Igniting the Pioneer Spirit

Microbiology Faculty

Stony Brook University's Department of Molecular Genetics and Microbiology in the School of Medicine invites applications for a tenure-track faculty position at the Assistant Professor level in the fields of virology and viral pathogenesis. Successful candidates will be expected to establish a vigorous extramural research program, direct graduate student and postdoctoral research, and participate in Departmental teaching and administrative responsibilities. The Department of Molecular Genetics and Microbiology and the adjacent Center for Infectious Diseases provide a highly interactive scientific community with world-class research facilities including two BSL-3 laboratories. The Department has training grants to support graduate students and postdoctoral fellows. The School of Medicine and Stony Brook University maintain core facilities that include imaging, sequencing, animal/transgenic, cell sorting, proteomics, microarray, bioinformatics, monoclonal antibodies, and cell culture.

Required: Applicants must have a Ph.D. or M.D./Ph.D. and have at least two years of postdoctoral experience. Outstanding candidates whose research is in the area of host response to viral infection are encouraged to apply. Special consideration will be given to candidates whose expertise will contribute to the study of human infectious disease. Specific areas of interest include, but are not limited to, RNA and DNA virology, virus-cell interactions, pathogenesis, and immunity to viruses.

The review of applications will begin immediately, and will continue until December 31, 2007, or until the position is filled.

To apply, send a C.V., a brief summary of accomplishments and future research interests (four pages total), and the names and contact information of three references to: Nancy C. Reich, Ph.D.
Chair of Search Committee, Department of Molecular Genetics and Microbiology
130 Life Sciences Building, Stony Brook University, SUNY
Stony Brook, NY 11794-5222

Fax: (631) 632-9797

Equal Opportunity/Affirmative Action Employer.
Visit *www.stonybrook.edu/jobs* for employment information.

STONY BROOK

MELANOMA RESEARCH FACULTY POSITIONS

The University of South Florida College of Medicine and the Donald A. Adam Comprehensive Melanoma Research Center at the H. Lee Moffitt Cancer Center and Research Institute are seeking laboratory-based faculty members with a Ph.D., M.D. or M.D.-Ph.D. in the Department of Interdisciplinary Oncology with an interest in melanoma research. The prospective candidates will be appointed at the Assistant, Associate or Full Professor level, and it is expected that they would establish an independent funded laboratory research program concentrating on translational melanoma investigation in the fields of genetics, signal transduction, microenvironment, apoptosis or the cell cycle.

An outstanding start-up plan is available, as well as a highly competitive salary package with excellent lab space. A specific attraction is the opportunity to interact with ongoing well-funded research programs in translational immunology/immunotherapy, drug development, population science and molecular oncology. The Comprehensive Melanoma Research Center will bring together clinicians and basic and translational scientists at Moffitt to aggressively pursue new ideas in the etiology, treatment and prevention of melanoma. At the H. Lee Moffitt Cancer Center, significant growth in basic and translational research, in laboratory space resources and faculty recruitment will occur in the next decade as a high priority.

The Associate/Full Professor must have a proven track record of independent research and demonstrated sustained extramural funding. In addition, the Associate Professor rank requires at least five years experience with continuing and productive service as an Assistant Professor. The Professor rank requires documentation of national recognition, leadership ability and at least five years experience with continuing and productive service as an Associate Professor. The positions are tenure earning and salary is negotiable.

Please reference position no. 14243. Interested candidates should send curriculum vitae and a brief statement of major academic interests in one single pdf document to Jeffrey Weber, M.D., Ph.D., c/o Kathy Jordan, Supervisor Recruitment & Appointment, Department of Interdisciplinary Oncology, 12902 Magnolia Dr., Tampa, FL 33612. For inquiries contact Dr. Weber at 813-745-2691, or email Jeffrey.Weber@moffitt.org. The positions are open until filled. Application review begins September 7, 2007.

H. LEE MOFFITT Cancer Center & Research Institute
The End Of Cancer Begins Here.
A National Cancer Institute Comprehensive Cancer Center
At the University of South Florida

USF HEALTH

USF Health is committed to increasing its diversity and will give individual consideration to qualified applicants for this position with experience in ethnically diverse settings, who possess varied language skills, or who have a record of research that supports/benefits diverse communities or teaching a diverse student population. The University of South Florida is an EO/EA/AA Employer. For disability accommodations, contact Kathy Jordan at (813) 745-1451 a minimum of five working days in advance. According to FL law, applications and meetings regarding them are open to the public.

www.moffitt.org

FACULTY POSITIONS

ECOLOGICAL/ENVIRONMENTAL FACULTY POSITION

The Department of Environmental Toxicology/Institute of Environmental and Human Health (TIEHH), Texas Tech University, is seeking a new faculty member at the **ASSOCIATE or FULL PROFESSOR** level with a focus on ecologically and or environmentally related diseases. The candidate will complement and expand areas of expertise represented within our environmental and human health research, teaching, and service programs (see **website: http://www.tiehh.ttu.edu** for program description). The successful applicant will have a Ph.D., an outstanding research, publication, and funding record, and is expected to build an active externally funded and internationally recognized program. The successful candidate should exhibit significant evidence of internal and external collaborative achievement. The ideal candidate should also be able to demonstrate excellence in teaching and be prepared to contribute to the education and training of graduate students.

Applications for this tenured or tenure-track position will be accepted until the position is filled. Applicants must submit online complete curriculum vitae, statement of teaching philosophy and interests, and a self-statement on how the candidate's proposed research will complement the current expertise of the Department and Institute (including startup requirements with annotated budget). Please process your application by accessing the Employment site at **website: http://jobs.texastech.edu** to reference requisition number 74859. Applicants should provide names and contact information for three colleagues willing to provide confidential letters of recommendation on their behalf. Letters of recommendation should be e-mailed to **e-mail: ernest.smith@tiehh.ttu.edu.**

Established as a joint venture between Texas Tech University and Texas Tech University Health Sciences Center, TIEHH pursues multidisciplinary research in the areas of environmental toxicology and human health. Emphasis is placed on developing innovative approaches to complex research questions that are of current importance, including the areas of biological and chemical threats.

Female and minority candidates are strongly encouraged to apply. TTU is Equal Opportunity/Affirmative Action Institution and actively seeks diversity among its employees.

BIOLOGY DEPARTMENT
Eukaryotic Developmental/Cell Biology

The Department of Biology seeks applicants for a tenure-track position to begin late August 2008. The successful candidate must have a Ph.D. and must have demonstrated excellence in undergraduate teaching; postdoctoral research experience preferred. Preference will be given to candidates working in animal or fungal systems who can take advantage of existing facilities. This person will teach introductory biology, molecular cell biology, genetics, and electives in area of expertise, and is expected to maintain an active research program that involves undergraduates. Colorado College is committed to increasing the diversity of its community and curriculum. Candidates are encouraged to identify the ways in which they can contribute to that goal. Application deadline is October 14, 2007. To apply send letter of application, curriculum vitae, graduate and undergraduate transcripts, statements of teaching philosophy and research interests, and three letters of reference to: **Dr. Marc Snyder, Department of Biology, Colorado College, 14 E. Cache la Poudre Street, Colorado Springs, CO 80903.** Colorado College is a highly selective national liberal arts college with a unique one-course-at-a-time curriculum. *The College is an Equal Opportunity Employer that does not discriminate on the basis of race, color, age, religion, sex, sexual orientation, national origin, or disability in its educational programs, activities, or employment practices.*

WAKE FOREST UNIVERSITY

ASSISTANT PROFESSOR, BIOLOGICAL CHEMISTRY
Wake Forest University

The Wake Forest University Department of Chemistry expects to fill two tenure-track positions at the rank of **ASSISTANT PROFESSOR** to begin August 2008. We are a Ph.D.-granting Department whose mission is to lead in undergraduate and graduate education and in research ventures that extend beyond the traditional boundaries of chemistry. Outstanding opportunities for multidisciplinary collaboration exist on our campus and with biomedical science departments at the Wake Forest University School of Medicine. Applicants must hold a Ph.D. (or equivalent) in chemistry or biochemistry, and will be expected to have a strong commitment to teaching biochemistry classes (and other classes according to their expertise) at the undergraduate and graduate levels. Applicants will also be expected to establish a vigorous, externally supported research program involving graduate and undergraduate students. Additional information about these positions can be found at **website: http://www.wfu.edu/academics/chemistry.** Applicants should submit a letter of application, curriculum vitae, copies of undergraduate and graduate transcripts, a two- to five-page statement of research goals, a one- to two-page statement of teaching philosophy, and three letters of recommendation to: **Chair, Biological Chemistry Search Committee, Department of Chemistry, Wake Forest University, Winston-Salem, NC 27109.** Applications will be accepted until November 1, 2007. *Wake Forest University is an Equal Opportunity, Affirmative Action Employer and is strongly committed to increasing the diversity of its faculty.*

FACULTY POSITION at the UNIVERSITY of PUERTO RICO

The Department of Biology of the University of Puerto Rico at Rio Piedras **(website: http://biology.uprrp.edu)** invites applications for a tenure-track position in cellular/molecular/biology/biochemistry, Investigators with expertise in cellular mechanisms (e.g. signal transduction, intracellular trafficking, protein metabolism) are particularly encouraged to apply. Candidates must hold a Ph.D. or equivalent and have postdoctoral experience. They are expected to develop active research programs and to teach at the graduate and undergraduate levels. Interested candidates should send resume, a statement of current and future research and teaching goals, representative publications and three letters of reference to: **Dr. James Ackerman, P.O. Box 23360, UPR Station, San Juan, PR 00931-3360** or **e-mail: ackerman.upr@gmail.com.** Applications will be reviewed from October 1, 2007, until the position is filled. *University of Puerto Rico is an Equal Opportunity Employer.*

University of Maryland Department of Kinesiology seeks a tenure-track **ASSISTANT PROFESSOR** to conduct research, supervise graduate students, and teach. Candidates must have postdoctoral training and a Ph.D. in exercise physiology or a closely related field. The candidate's research must emphasize mechanistic endpoints related to physical activity. Application deadline is November 1, 2007, with a start date of August 2008. For more information contact **James Hagberg, Ph.D. (e-mail: hagberg@umd.edu)** or see the Department **website: http://www.hhp.umd.edu/KNES/.** *Women and minorities are strongly encouraged to apply.*

TWO TENURE-TRACK FACULTY POSITIONS
Exercise Physiology
West Virginia University School of Medicine
Division of Exercise Physiology

In an expanding commitment to research excellence in cardiovascular and muscle biology, West Virginia University School of Medicine invites applications from outstanding scientists for two new tenure-track faculty positions as **ASSISTANT, ASSOCIATE or FULL PROFESSOR,** in the Division of Exercise Physiology **(website: http://www.hsc.wvu.edu/som/ep/availablePositions.asp).**

Applicants must hold a Ph.D., M.D. or equivalent and have current transferable extramural federal funding as a Principal Investigator (e.g., NIH R01). We are seeking candidates who use modern research approaches to address significant clinical/translational or basic problems in muscle biology, cardiovascular diseases, or diabetes, and whose research aligns with the Center for Interdisciplinary Research in Cardiovascular Sciences or another research center that has been identified in the West Virginia University School of Medicine.

Appointees will be expected to maintain an independent, extramural nationally funded research program. The successful candidates will be encouraged to participate in graduate education through developing a graduate course in their area of expertise and mentoring doctoral students. For qualified applicants, administrative leadership opportunities exist. A generous startup package, competitive salary commensurate with experience, and independent laboratory space will be provided.

Qualified individuals should submit complete curriculum vitae, a brief description of research interests, and the names, addresses (including e-mail), and telephone numbers of three references to: **John M. Hollander, Ph.D., Search Committee Chair, Division of Exercise Physiology, West Virginia University School of Medicine, P.O. Box 9227, Morgantown, WV 26506-9227.** Please submit materials electronically to **e-mail: jhollander@hsc.wvu.edu** and please copy all documents to **e-mail: astannard@hsc.wvu.edu** and **e-mail: rgmiller@hsc.wvu.edu.** Review of applications will begin September 30, 2007, and continue until the positions are filled. One of the positions is available January 1, 2008, and the other position is available July 1, 2008.

WVU is an Equal Opportunity/Affirmative Action Employer.

Muhlenberg College Biology Department announces two tenure-track **ASSISTANT PROFESSOR** positions beginning fall 2008, in physiological/behavioral ecology (pending approval) and in animal physiology. Strong commitment to teaching and research in a small liberal arts college environment required. Ecology teaching responsibilities include intro course for majors in the area of evolution/diversity/ecology, general physiology, and upper-level courses in area of expertise. Physiology teaching responsibilities include introductory course for majors in the area of animal and plant organismal biology, general physiology, and an upper-level course in area of expertise. Candidates that can interface with interdisciplinary environmental science and/or neuroscience programs welcomed. The College's new science facility offers state-of-the-art teaching and research laboratory spaces. Ph.D. required (postdoctoral experience preferred) as are a record of excellent teaching and an active research program that can involve students. To apply, send letter of application, curriculum vitae, statement of teaching and research interests, evidence of teaching excellence, and three reference letters to: **Dr. Richard Niesenbaum, Chair of Ecology Search, Muhlenberg College, Allentown, PA 18104;** or to: **Dr. Marten Edwards, Chair of Physiology Search, Muhlenberg College, Allentown, PA 18104.** Applicant review begins October 15, 2007, and continues until the positions are filled. *Muhlenberg College is an Equal Opportunity Employer.*

Penn
UNIVERSITY of PENNSYLVANIA

Institute for Diabetes, Obesity and Metabolism, Assistant/Associate Professor Tenure Track

The Institute for Diabetes, Obesity and Metabolism (IDOM) at the University of Pennsylvania's School of Medicine seeks candidates for an Assistant or Associate Professor position in the tenure track. Rank will be commensurate with experience. Applicants must have an M.D, Ph.D. or M.D./Ph.D. degree and have demonstrated excellent qualifications in Education and Research. The faculty appointment will be in the appropriate Basic Science Department and/or the Department of Medicine.

The successful applicant will receive an excellent start-up package and move into newly renovated space in a superb scientific environment.

Qualified applicants must have demonstrated research productivity related to diabetes or obesity. We are particularly interested in individuals who will complement existing strengths of the Penn IDOM. For more information: visit IDOM website at **http://www.med.upenn.edu/idom/**. The successful candidate is expected to develop an independently funded research program. Qualifications and experience in teaching required.

Please send curriculum vitae, letter of research interest and three letters of reference to:

Mitchell A. Lazar, M.D., Ph.D.
Professor of Medicine and Chief of Endocrinology, Diabetes and Metabolism
Director, Institute for Diabetes, Obesity and Metabolism
University of Pennsylvania School of Medicine
700 Clinical Research Building
415 Curie Boulevard
Philadelphia, PA 19104-6149

The University of Pennsylvania is an Equal Opportunity, Affirmative Action Employer.
Women and minority candidates are strongly encouraged to apply.

UNIVERSITY OF CALIFORNIA SAN FRANCISCO SYSTEMS/QUANTITATIVE BIOLOGY

The California Institute for Quantitative Biomedical Research (QB3) at UCSF seeks candidates for multiple tenure track faculty positions at the Assistant Professor level. We seek exceptional individuals working in the area of Systems Biology, broadly defined, working on quantitative and computational analysis of biological systems and networks.

Candidates are expected to hold a PhD or MD degree, or equivalent, and to have demonstrated achievement in their fields. The successful candidate will be expected to establish a dynamic research program and to be an excellent teacher in both graduate and professional school courses.

Applicants should submit a curriculum vitae, 1-2 page summary of research accomplishments, a 1-2 page description of future research plans, and copies of major publications. Applicants should also have three to five letters of recommendation. Please send applications and reference letters to: **Chair, Search Committee, c/o Ms. Leslie Spector, UCSF, BH-403E, 1700-4th St, MC 2542, San Francisco, CA 94158**. Deadline for submissions: **November 1, 2007**.

We encourage women and minorities to apply. The University of California San Francisco is an Equal Opportunity/ Affirmative Action Employer.

MICHIGAN STATE UNIVERSITY

Molecular Oncology, Endowed Professorship

The Walter F Patenge Health Sciences Chair is an endowed professorship at Michigan State University in East Lansing, Michigan. This tenured, laboratory-based, research-oriented position will be filled by a senior-level molecular oncologist with an outstanding record of funded research in the area of human cancer.

The Patenge Chair search is part of a coordinated, well-funded initiative to enhance research on human diseases at MSU. The Patenge Professor will have access to university genetics diagnostics labs, strong epidemiology and neuroscience programs, an interdepartmental graduate program in genetics, and strength in research in a wide array of basic sciences. MSU provides excellent research support facilities in genomics, proteomics, and microscopy.

MSU's basic science departments report administratively through the various University Colleges, whose students and research programs they serve. This administrative structure promotes a highly collegial and highly interdisciplinary environment-with many collaborative opportunities. The Patenge Professor has access to the resources of MSU's two community-based medical schools (D.O. and M.D.), and MSU's research-oriented College of Nursing - all of which are associated with large health care systems located throughout Michigan.

The Patenge Professor will receive substantial laboratory space in MSU's state-of-the-art Carcinogenesis Laboratory, a suitable setup package, and annual interest from the endowment for furthering the candidate's research. The successful candidate will be appointed in one or more of the following departments: Microbiology & Molecular Genetics; Biochemistry & Molecular Biology; Physiology; or Pharmacology & Toxicology. A candidate who holds a professional degree will be jointly appointed in an appropriate clinical department. Salary will be commensurate with the rank of endowed professor.

QUALIFICATIONS: The successful candidate will have a superior record of peer-reviewed publication and will possess a research and/or medical degree (e.g., Ph.D., Sc.D., D.O., M.D.). The successful candidate will have a background that demonstrates his/her ability to work synergistically with both scientific and medical colleagues.

APPLICATIONS: This position will remain open until filled. Send a letter of application, a vita that demonstrates success at obtaining external research funding, and a statement of research goals along with pertinent reprints and the contact information for three referees (address, e-mail, and phone). These materials should be addressed to: **Chairperson, Patenge Search Committee; A314 East Fee Hall; East Lansing, MI 48824.** E-mailed submissions in PDF format are welcomed and encouraged at **patenge.search@hc.msu.edu**.

Michigan State University is committed to achieving excellence through cultural diversity. The university actively encourages applications and/or nominations from women, persons of color, veterans and persons with disabilities.

MSU IS AN AFFIRMATIVE ACTION, EQUAL OPPORTUNITY EMPLOYER.

FACULTY POSITIONS

ASSISTANT and/or ASSOCIATE PROFESSOR of HUMAN GENETICS

The Department of Human Genetics at the University of Utah School of Medicine is continuing a new major expansion, recruiting three new investigators over the next three years to build upon existing strengths in human genetics and developmental biology.

We are seeking outstanding applicants at the level of **ASSISTANT and/or ASSOCIATE PROFESSOR** in the broad fields of genetics and functional genomics, including but not limited to human genetics, genetic approaches to complex disease, population genetics, behavioral genetics, regenerative medicine, developmental genetics, and animal models of human disease and development. Our Department has a strong history in human genetics and resources, such as the Utah Population Data Base, that are unique in the world. These resources have created a highly productive and collaborative environment between researchers, clinicians, and the community.

Creative scientists with a record of achievement and commitment to excellence in both research and teaching are encouraged to apply. Successful candidates will receive a substantial startup package and enjoy a stimulating and supportive research environment.

Applicants should submit curriculum vitae, a summary of research plans, relevant reprints and/or preprints, and three letters of reference to:

Dr. Mario R. Capecchi
Co-Chair, Department of Human Genetics
Howard Hughes Medical Institute
University of Utah School of Medicine
15 North 2030 East, Room 2130
Salt Lake City, UT 84112-5330

Application materials, including letters of reference, should be submitted by November 9, 2007.

The University of Utah is an Equal Opportunity/Affirmative Action Employer, encourages nominations and applications from women and minorities, and provides reasonable accommodation to the known disabilities of applicants and employees.

FACULTY POSITIONS in MOLECULAR, CELLULAR, and DEVELOPMENTAL BIOLOGY
University of Michigan

The Department of Molecular, Cellular, and Developmental Biology at the University of Michigan solicits applications for faculty positions. We are open to considering outstanding basic scientists in any area of research that fits with the mission of the Department, but areas that will receive particular emphasis for hiring in the coming year are (1) microbiology, (2) animal physiology, and (3) plant biochemistry. For further information about specific areas of interest, please see our web page (**website: http://www.mcdb.lsa.umich.edu**).

We anticipate hiring at the **ASSISTANT PROFESSOR** level, but appointment at a more senior level is possible for applicants with suitable experience. Successful candidates will be expected to establish a vigorous, extramurally funded research program and to be involved in instruction of both undergraduate and graduate students.

To apply, candidates should send a cover letter, curriculum vitae, copies of reprints, a brief summary of recent research accomplishments, a statement of future research plans, and a statement of teaching interests and philosophy. Senior candidates should also provide evidence of teaching excellence. Please indicate in the cover letter which, if any, of the areas of emphasis your research falls into. Candidates for appointment as an Assistant Professor should have at least three letters of reference sent immediately to the Department. All materials should be sent to: **Search Committee, Department of Molecular, Cellular, and Developmental Biology, University of Michigan, 830 N. University Avenue, Ann Arbor, MI 48109-1048** or submitted via **e-mail: mcdb-search@umich.edu.** To ensure full consideration, applications and letters of reference should be received by October 12, 2007.

Women and minorities are encouraged to apply. The University of Michigan is supportive of the needs of dual career couples and is an Equal Opportunity/Affirmative Action Employer.

VIRGINIA COMMONWEALTH UNIVERSITY
Department of Chemistry

The Department of Chemistry at Virginia Commonwealth University invites applications for a tenure-track position in physical chemistry, to begin in fall 2008, contingent upon funding. Applications at the **ASSISTANT PROFESSOR** level are preferred but any rank will be considered. The successful candidate will be expected to develop and maintain a funded, nationally recognized research program, and teach undergraduate and graduate courses in general and physical chemistry. The candidate's research interests will strengthen the Department's current initiatives in material science and chemical biology. All areas of physical chemistry will be considered but candidates with research related to these areas (nanomaterials and/or biophysical) and using ultrafast spectroscopy would be of interest. A Ph.D. in chemistry is required, and postdoctoral experience is desirable. Applicants should send curriculum vitae, a description of proposed research, and estimated startup costs, and arrange for three letters of recommendation to be sent to: **Prof. M.S. El-Shall, Chair of the Physical Search Committee, Department of Chemistry, P.O. Box 842006, Virginia Commonwealth University, Richmond, VA 23284-2006.** Review of applications will begin immediately. *Virginia Commonwealth University is an Equal Opportunity/Affirmative Action Employer. Women, minorities and persons with disabilities are encouraged to apply.*

FACULTY and STAFF POSITION

University of Missouri, Columbia, Department of Psychological Sciences seeks applications for several positions related to our new brain imaging center. The **MILLER FAMILY CHAIR in COGNITIVE NEUROSCIENCE** is open to Full Professors and advanced Associate Professors, or nonacademic equivalents. We expect this endowed position to be filled by a tenured faculty member, who will have the opportunity to direct the research-dedicated Brain Imaging Center.

An additional **POSITION in COGNITIVE/AFFECTIVE NEUROSCIENCE** is to be filled at the tenured or tenure-track, **ASSOCIATE or ASSISTANT PROFESSOR** level. We also are recruiting an **MR PHYSICIST** (Engineers will also be considered) and an **MR TECHNOLOGIST** to be filled as continuing, nontenure-track staff positions. Responsibilities would include working with faculty to optimize the quality of MR imaging and research.

Send your application to: **Search Committee Chair (naming the appropriate position), Department of Psychological Sciences, McAlester Hall, University of Missouri, Columbia, MO 65211.** Electronic applications or enquiries can be sent to **Dr. Nelson Cowan (e-mail: cowann@missouri.edu; telephone: 573-882-4232)** for the Miller Chair position, **Drs. Steve Hackley (hackleys@missouri.edu; telephone: 573-882-3277)** and **Jeffrey Rouder (rouderj@missouri.edu; telephone: 573-884-4679)** for the cognitive/affective neuroscience position, or **Dr. Steve Hackley (hackleys@missouri.edu; telephone: 573-882-3277)** for the staff positions.

Applications should include a cover letter describing research and teaching interests; curriculum vitae; three to five representative reprints; and letters or contact information for three referees. Applications will be evaluated beginning November 1, 2007, and continuing until the positions are filled. **Website: http://psychology.missouri.edu/**

The University of Missouri does not discriminate on the basis of race, color, religion, national origin, ancestry, sex, age, and disability, status as a disabled veteran or veteran of Vietnam era and is an Equal Opportunity/Affirmative Action Employer.

EXPERIMENTAL ATOMIC, MOLECULAR and OPTICAL PHYSICS

The Physics Department, the James Franck Institute, and the Enrico Fermi Institute at the University of Chicago invite applications for a tenure-track faculty appointment in the general area of experimental atomic, molecular, and optical physics (AMO). The appointment will start in the fall of 2008. We encourage applications from candidates with an outstanding record of research in areas such as ultracold atoms and molecules, precision measurements, quantum optics, quantum information, as well as ultrafast laser physics. The successful candidate must have a doctoral degree in physics or related fields, and is expected to establish an independent research program while effectively contributing to the Department's undergraduate and graduate teaching programs.

The appointment is expected to be at the **ASSISTANT PROFESSOR** level. Appointment at the level of **ASSOCIATE PROFESSOR or FULL PROFESSOR** is possible for exceptionally well-qualified candidates. Applicants should send curriculum vitae, a list of publications, a brief research statement, and arrange to have at least three reference letters sent to:

Professor Robert Wald, Chairman
Department of Physics, KPTC 201
The University of Chicago
5720 S. Ellis Avenue
Chicago, IL 60637

E-mail should be sent to **Ms. Pat Plitt** at **e-mail: pplitt@uchicago.edu.**

Review of applications will start in the fall of 2007, and will continue until the position is filled. To ensure full consideration, applications should be received no later than November 1, 2007. *The University of Chicago is an Equal Opportunity, Affirmative Action Employer.*

TENURE-TRACK POSITION in CELL/ MOLECULAR BIOLOGY
University of Toledo

The Department of Biological Sciences at the University of Toledo is seeking to fill a tenure-track **ASSISTANT PROFESSOR** faculty position as part of a major hiring initiative. Departmental research strengths include cellular immunology, cancer biology, nematode molecular biology, molecular neuroscience, and plant biology, and other departments in the College of Medicine on the nearby Health Science Campus of the university complement these areas. The new position will enhance existing research strengths. Facilities include a modern research complex with state-of-the-art laboratories and outstanding instrumentation centers with plans under way for a new science building. Applicants must have a Ph.D. and postdoctoral experience. Successful candidates should have or will be expected to develop an externally funded research program and will participate in undergraduate and graduate instruction. The Department offers the B.S., M.S., and Ph.D. degrees. Additional information is available on the departmental **website: http://www.biosciences.utoledo.edu.**

Salary and startup funds are competitive. Review of applications will begin October 15, 2007, and continue until the position is filled. The starting date for this position will be August 2008. Interested candidates should send a letter of application, curriculum vitae, statements of teaching and research interests, and arrange to have three letters of recommendation sent to: **Chair, Faculty Search Committee, Department of Biological Sciences, M.S. 601, University of Toledo, Toledo, OH 43606-3390.** E-mail inquiries may be directed to **e-mail: john.plenefisch@utoledo.edu** or **patricia.komuniecki@utoledo.edu.**

Qualified women and minorities are encouraged to apply. The University of Toledo is an Affirmative Action/Equal Opportunity Employer Minorities/Females/Persons with Disabilities/Veterans.

WASHINGTON STATE UNIVERSITY

ASSISTANT/ASSOCIATE PROFESSOR
Pharmaceutical Sciences/Bioengineering/Nanomedicine

The Department of Pharmaceutical Sciences at Washington State University in Pullman, WA (**www.pharmacy.wsu.edu/PharmSci/**) invites applications for a full-time, 12-month tenure-track position at the rank of Assistant or Associate Professor to begin July 1, 2008 or earlier. **Qualifications:** Applicants must have an earned doctorate in pharmaceutical sciences, bioengineering or a related discipline before date of hire. **Responsibilities:** Candidates will be expected to: (a) teach at both the professional and graduate levels; (b) develop and maintain an extramurally funded research program; and (c) share in service to the Department, College and University. The successful candidate will receive a competitive start-up package and will be expected to establish an outstanding research program that will attract continued extramural funding. Preference will be shown to those whose research aligns with nanomedicine and delivery systems for drugs, genes, peptides, nucleic acids, or viral delivery. The successful candidate should have excellent communication and interpersonal skills, collegiality, and a strong global perspective. He/she should demonstrate the ability to contribute effectively in the department's teaching missions at both professional and graduate levels.

Screening of applicants will begin **November 1, 2007**. The application must include a letter of interest; *curriculum vitae*; statements of research goals and teaching interests; as well as the names, email addresses, and contact information for three references. Send applications to: **Ms. Paula Marley, Principal Assistant, Dept. of Pharmaceutical Sciences, College of Pharmacy, Washington State University, Pullman, WA 99164-6534. bbr@wsu.edu; Phone: (509) 335-5545; Fax: (509) 335-5902.** Applications should be mailed or emailed as PDF documents.

EO/AA/ADA

JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

JHMRI JOHNS HOPKINS MALARIA RESEARCH INSTITUTE

STRUCTURAL BIOLOGIST
Johns Hopkins Malaria Research Institute
Department of Biochemistry and Molecular Biology
Department of Molecular Microbiology and Immunology

The Johns Hopkins Malaria Research Institute and the Departments of Biochemistry and Molecular Biology and Molecular Microbiology and Immunology invite applications for a tenure track faculty position in the area of structural biology. Preference will be given to candidates at the assistant professor level, but candidates at more senior levels will be considered. We particularly seek applicants whose research employs x-ray crystallographic and biophysical approaches to address fundamental questions in microbiology or immunology.

Extensive core facilities are available, including a biophysics facility with equipment for crystallography, calorimetry and spectroscopy. A competitive start-up package, salary and benefits will be provided. Individuals will be expected to develop independent research programs within an interactive environment of investigators interested in the pathogenesis of viral, bacterial and parasitic diseases and the biochemistry and molecular biology of fundamental cellular processes. Opportunities exist for interaction with the vibrant Johns Hopkins biophysical research community and graduate training programs. Applicants must have a PhD, MD, or equivalent degree and appropriate post-doctoral experience.

Review of applications will begin **November 1, 2007** and will continue until the position is filled. Applicants should provide curriculum vitae, description of research interests and three letters of reference to: **Susan Booker, JHMRI Coordinator, Johns Hopkins Bloomberg School of Public Health, Room E5132, 615 North Wolfe St, Baltimore, MD, 21205; V. 410-502-3377; F. 410-955-0105; sbooker@jhsph.edu**. For information on JHMRI, BMB and MMI faculty and research programs, please visit **www.jhsph.edu**.

The Johns Hopkins University actively encourages interest from women and minorities and is an Affirmative Action/Equal Opportunity Employer.

Weill Cornell Medical College in Qatar

FACULTY POSITIONS

In a pioneering international initiative, Cornell University established the Weill Cornell Medical College in Qatar (WCMC-Q) through a unique partnership with the Qatar Foundation for Education, Science and Community Development. Located in Doha, Qatar and in its sixth year of operation, Weill Cornell Medical College in Qatar seeks candidates for faculty positions to teach in Doha in:

PHYSIOLOGY

Following a two-year Pre-medical Program, the inaugural class is in the final year of the traditional four-year education program leading to the Cornell University M.D. degree which they will receive in May 2008. The medical program at WCMC-Q replicates the admission standards and the innovative problem-based curriculum that includes, among other things, integrated, multidisciplinary basic science courses that are the hallmark of Weill Cornell Medical College in New York.

Faculty, based in Doha, will be expected to teach their specialty and to contribute to the academic life of the Medical College. This unique program provides the successful applicant with the opportunity to leave his/her mark on a pioneering venture. A state of the art research program, to be housed in WCMC-Q and focused on genetics and molecular medicine and women and children's health will be initiated Fall 2007. In addition to fulfilling their primary obligation of teaching, selected candidates will have the opportunity to participate in existing research projects. Opportunities to apply for research funding on a competitive basis will be available in Qatar. Teaching and research facilities are situated within a brand new building designed to Cornell specifications and located in Education City in Doha amongst other American universities.

All faculty members at WCMC-Q are appointed by the academic departments at Weill Cornell Medical College in New York.

Further details regarding the WCMC-Q program and facilities can be accessed at:

www.qatar-med.cornell.edu

Candidates should have a M.D., Ph.D., or M.D./Ph.D. or equivalent terminal degree. The successful candidate will have strong teaching credentials and experience in teaching medical students. Salary is commensurate with training and experience and is accompanied by an attractive foreign-service benefits package. Qualified applicants should submit a letter of interest outlining their teaching and research experience and curriculum vitae to:

facultyrecruit@qatar-med.cornell.edu

***Please quote Faculty Search #07-007-sci on all correspondence**

Cornell University is an equal opportunity, affirmative action educator and employer.

The screening of applications will begin immediately and continue until suitable candidates are identified.

Please note, due to the high volume of applications, only short-listed candidates will be contacted.

FACULTY POSITIONS

TENURE-TRACK IMMUNOLOGY FACULTY POSITION

The Department of Cell Biology, Neurobiology, and Anatomy at Loyola University Chicago Medical Center, Stritch School of Medicine, is recruiting a tenure-track **IMMUNOLOGIST.** Investigators who focus on mechanisms governing the aging of the immune system are strongly encouraged to apply; however, other aspects of immune function will also be considered. Existing strengths in the Department include: T and B cell development in aging; effector functions of T helper cells in neuronal repair; influence of alcohol, age, and gender on innate immunity; roles of chemokines and cytokines in the development and management of chronic pain; and roles of hormones and alcohol in the development and function of cells of the nervous system. Loyola University Medical Center supports basic and translational research by providing state-of-the-art equipment and core facilities including fluorescence activated cell sorter, imaging, molecular, statistics, and animal care. Numerous opportunities exist for collaborations not only within the Department but also with clinicians and faculty members in the Interdisciplinary Research Institutes and Programs: Neuroscience, Shock Trauma, Infectious Disease and Immunology, Alcohol Research, and Immunology and Aging. Potential candidates are expected to establish an independent, extramurally funded research program and to participate in teaching medical and graduate students. Appointments are for 12 months with a competitive startup package and laboratory space; rank will be commensurate with qualifications. Applicants should provide curriculum vitae, a statement of research interests, and have three letters of support submitted directly to the **Chair.** These materials should be sent **via e-mail: pwitte@lumc.edu** and by post to: **Pamela Witte, Ph.D., Department of Cell Biology, Neurobiology and Anatomy, Loyola University Stritch School of Medicine, 2160 S. First Avenue, Maywood, IL 60153.** For more information, visit our **website: http://www.luhs.org/depts/cbna/mainpage2.htm.** Review of applications will begin November 15, 2007.

The Loyola University of Chicago Stritch School of Medicine is an Affirmative/Equal Opportunity Employer and encourages applications from women and minorities.

TENURE-TRACK BIOCHEMIST, Hamilton College, invites applications for a tenure-track position in biochemistry beginning July 2008. An entry-level appointment is targeted, but appointment of a senior scholar is possible. Ph.D. and postdoctoral or equivalent experience required.

Applicants must be committed to undergraduate education with interest in teaching an increasingly diverse student population and demonstrate excellence, or the potential for excellence, in teaching and research with undergraduates. Primary teaching responsibilities will be in biological chemistry with additional responsibilities in introductory chemistry, research methods, and other courses in the candidate's areas of expertise. The successful candidate will be expected to guide student research during the summer and advise the required Senior Project during the academic year. Excellent startup support will be provided. You will join a group of committed teacher/scholars who insist on excellence in teaching and have a passion for educating students through one-on-one mentoring of research. We work in a supportive collegial environment with superb administrative support in a new state-of-the-art facility.

Further information about Hamilton and the Department can be found at **website: http://www.chem.hamilton.edu.** Please send curriculum vitae, undergraduate and graduate transcripts, statements describing teaching interests and research plans, and arrange for three letters of recommendation to be sent by October 12, 2007, to: **Karen S. Brewer, Chair, Department of Chemistry, Hamilton College, 198 College Hill Road, Clinton, NY 13323.** *Hamilton College is an Equal Opportunity, Affirmative Action Employer and is committed to diversity in all areas of the campus community. Hamilton provides domestic partner benefits.*

FACULTY POSITIONS

OREGON HEALTH & SCIENCES UNIVERSITY

The Oregon Health & Sciences University (OHSU) Department of Behavioral Neuroscience invites applications for a **TENURE-TRACK JUNIOR FACULTY POSITION.** We seek an outstanding applicant with a Ph.D. or equivalent degree, postdoctoral experience, and a strong publication record. Evidence of extramural research funding is desirable. The position is not limited in area of expertise; however, special consideration will be given to individuals with interests in the area of alcohol and drug abuse. Individuals with expertise in any area of genomics, including human genetics, are especially encouraged to apply. *The successful applicant must be a U.S. citizen or permanent resident.* OHSU places a high priority on cultural diversity; thus, we seek candidates with a demonstrated sensitivity to and understanding of the diverse academic, socioeconomic, cultural, disabled and ethnic backgrounds of OHSU's students and employees. The salary and startup package is very competitive. The review of applications will begin in September 2007. The position will remain open until filled. Send cover letter, curriculum vitae, statement of research interests, and contact information for three references to: **Rebecca Salzer (e-mail: salzerr@ohsu.edu), Department Administrator, Oregon Health & Science University, Department of Behavioral Neuroscience, L-470, 3181 S.W. Sam Jackson Park Road, Portland, OR 97239-3098. Website: http://www.ohsu.edu/behneuro/.**

OHSU is an Affirmative Action, Equal Opportunity Employer. Women, minorities, disabled persons, Vietnam era and disabled veterans are encouraged to apply. OHSU is a smoke-free workplace.

EVOLUTIONARY DEVELOPMENTAL BIOLOGIST
Bryn Mawr College

The Department of Biology invites applications for a tenure-track position in evolutionary developmental biology at the rank of **ASSISTANT PROFESSOR,** beginning August 2008. We seek as a colleague someone who will thrive in an environment that combines teaching and research. The successful candidate is expected to teach at all levels of the curriculum and establish an externally funded research program that provides rigorous collaborative research projects for undergraduates. Individuals who study animal and/or plant development model systems with a strong evolutionary context are encouraged to apply. A Doctorate and at least one year of postdoctoral experience are required.

Please send a letter of application, curriculum vitae, a description of research plans that addresses the role of undergraduates in your research, and a statement of teaching philosophy that includes areas of teaching interests, and arrange for three letters of recommendation to be sent by September 21, 2007, to: **Chair, Biology Search, Department of Biology, Bryn Mawr College, 101 N. Merion Avenue, Bryn Mawr, PA 19010-2899.** (No electronic submissions, please.)

Located in suburban Philadelphia, Bryn Mawr College is a highly selective liberal arts college for women who share an intense intellectual commitment, a self-directed and purposeful vision of their lives, and a desire to make meaningful contributions to the world. Bryn Mawr comprises an undergraduate college with 1,200 students, as well as coeducational graduate schools in some humanities, sciences, and social work. The College supports faculty excellence in both teaching and research, and participates in consortial programs with the University of Pennsylvania, and Haverford and Swarthmore Colleges. *Bryn Mawr College is an Equal Opportunity, Affirmative Action Employer. Minority candidates and women are especially encouraged to apply.*

FACULTY POSITIONS

INORGANIC CHEMISTRY
COLLEGE of NATURAL SCIENCES and MATHEMATICS
Department of Chemistry and Biochemistry
California State University, Fullerton

The Department of Chemistry and Biochemistry at California State University, Fullerton, invites applications for a tenure-track position in inorganic chemistry, preferably at the **ASSISTANT PROFESSOR** level, to begin in August 2008. A willingness to engage in collaborative research and/or interdisciplinary research in related fields is desirable. The successful applicant must have a Ph.D. in chemistry, biochemistry, or a related field. Postdoctoral or comparable research experience is strongly preferred. Applicants must have the potential to develop a vigorous research program involving undergraduate and graduate students that attracts external funding and leads to refereed publications. Research interests in all areas of inorganic chemistry will be considered. The successful candidate must be committed to excellence in teaching. Primary teaching responsibilities will be in the core lecture and laboratory courses for inorganic chemistry and related courses in other chemistry disciplines, at the undergraduate and graduate levels.

Information about the University and Department as well as full information on the advertised position is available online at **websites: http://chemsrvr2.fullerton.edu/DeptWebsite/directory.html and http://diversity.fullerton.edu/.** Applicants should send hard copies of (a) a cover letter explaining how they meet the qualifications outlined above, (b) detailed curriculum vitae, (c) a statement of teaching philosophy, (d) a statement of research plans and goals, and (e) copies of representative publications. They must also arrange to have sent signed letters of recommendation from three references familiar with their teaching and research potential. Please send these documents to: **Chair, Inorganic Chemistry Search Committee, c/o Nathalie Allen, Department of Chemistry and Biochemistry, California State University, Fullerton, P.O. Box 6866, Fullerton, CA 92834-6866.** Review of applications will begin October 1, 2007, and will continue until the position is filled. *CSUF is an Equal Employment Opportunity/Title IX/503/504/VEVRA/ADA Employer. Women and minority candidates are particularly encouraged to apply.*

TENURE-TRACK FACULTY POSITIONS

The Department of Biochemistry and Molecular Biology at the Uniformed Services University of the Health Sciences in Bethesda, Maryland, is recruiting one or more faculty members to tenure-track positions at the **ASSISTANT or ASSOCIATE PROFESSOR** level. Candidates are expected to develop independent, externally funded research programs, and senior-level applicants will have established such programs. Individuals working in any area of molecular biology or biochemistry will be considered, and applications from individuals using molecular modeling, bioinformatics, or structural methods to address biologically important problems are especially encouraged. All faculty participate in the training of graduate and medical students. Information about our Department, including descriptions of our present research programs, can be found at **website: http://bio.usuhs.mil.** Further questions can be addressed to **e-mail: biofacultysearch@usuhs.mil.** Applicants should submit curriculum vitae including a description of research interests to:

Faculty Search Committee
Department of Biochemistry and Molecular Biology
Uniformed Services University of the Health Sciences
4301 Jones Bridge Road
Bethesda, MD 20814

and should arrange for letters of recommendation to be sent. Review of applications will begin on November 1, 2007. *Preference will be given to U.S. citizens and permanent residents. USUHS is an Equal Opportunity Employer.*

FACULTY POSITION
CENTER FOR MICROBIAL PATHOGENESIS

The CENTER FOR MICROBIAL PATHOGENESIS at Columbus Children's Research Institute, Columbus Children's Hospital, and the Department of Pediatrics, College of Medicine, The Ohio State University seek PhD, MD, or MD/PhD candidates for a tenure-track position at the Assistant or Associate Professor rank to develop and conduct an independent research program in the fields of cellular and molecular microbiology as well as innate and acquired immunity. One area of specific emphasis is the study of bacterial pathogens causing disease in the gastrointestinal tract. Research space is available within the Columbus Children's Research Institute. This recruitment is part of a larger multi-year planned expansion of research initiatives by the institution and includes the 2004 completion of a 160,000-square-foot five-story research building that houses 48 state-of-the-art laboratory modules. Additional research space is slated to open in 2008. The Institute is equipped with leading-edge assets to facilitate collaboration and success, including animal facilities in addition to DNA sequencing, flow cytometry, informatics, histopathology, transgenic, microarray, ES cell, and transgenic cores. Joint appointments within graduate departments of The Ohio State University are available.

For more information, please visit our website at **www.ccri.net**.

Address correspondence with three references and curriculum vitae to:

Lauren O. Bakaletz, Ph.D.
Director, Center for Microbial Pathogenesis
Columbus Children's Research Institute
700 Children's Drive, Rm. W591
Columbus, OH 43205
Phone: (614) 722-2915 FAX: (614) 722-2818
E-mail: bakaletl@ccri.net

The Ohio State University is an Equal Opportunity/ Affirmative Action Employer. Qualified women, minorities, Vietnam-era veterans, disabled veterans, and the disabled are encouraged to apply.

THE OHIO STATE UNIVERSITY

COLUMBUS Children's RESEARCH INSTITUTE

Karolinska Institutet

PROFESSOR IN INFECTIOUS EPIDEMIOLOGY

Karolinska Institutet invites applications for a position as professor in Infectious Epidemiology.

For further details please contact Professor Hans-Gustaf Ljunggren, phone: +46 8 585 896 84, email: **Hans-Gustaf.Ljunggren@ki.se** or the SACO union representative Michael Fored, phone: +46 8 517 791 81, email: **Michael.Fored@ki.se**

Please state your qualifications in accordance with the Karolinska Institutet qualification portfolio available on the Web page **http://info.ki.se**

Deadline for applications is **October 10, 2007**. **Reference no 1368/ 07-221**, Registrar, Karolinska Institutet, SE-171 77 Stockholm, Sweden.

For the entire advertisement please look at **http://jobb.ki.se/internal/general/starteng.asp**
E-mail: **Registrator@ki.se**

MICROBIAL PATHOGENESIS

FACULTY POSITIONS – OPEN RANK

CENTER FOR MOLECULAR AND TRANSLATIONAL HUMAN INFECTIOUS DISEASE RESEARCH

THE METHODIST HOSPITAL RESEARCH INSTITUTE

The Methodist Hospital Research Institute (TMHRI) at The Methodist Hospital (TMH) in Houston, Texas, seeks several exceptional scientists studying the molecular basis of microbial pathogenesis. We are especially interested in senior investigators with established research programs.

The Methodist Hospital System consists of 1,450 beds, including 950 located in the Texas Medical Center in Houston. Collaborative opportunities are available with our partners at Weill Cornell College of Medicine and New York-Presbyterian Hospital in New York City, the University of Houston, and other local institutions.

The Hospital has entered an unprecedented expansion phase that includes building a 420,000-square-foot state-of-the-art research building with bio-containment and animal facilities, and a 750,000-square-foot ambulatory care building, both designed to foster interdisciplinary collaborative research.

Candidates using new or proven technologies to study molecular events occurring at the host-pathogen interface are preferred, but all outstanding investigators are encouraged to apply. Successful applicants will be responsible for establishing or expanding nationally recognized, externally funded research programs.

Applicants must have an advanced degree (PhD, DVM, MD, or MD/PhD). Successful applicants will receive an outstanding recruitment package. Interested individuals should send via e-mail, by October 15, 2007, a curriculum vitae; description of research interests, future directions, and grant funding information; and the names of at least three references to:

James M. Musser, M.D., Ph.D.
c/o Ms. Irene Harrison
E-mail: iaharrison@tmhs.org
Co-Director and Executive Vice President,
The Methodist Hospital Research Institute
6565 Fannin St., Mail Stop B490
Houston, TX 77030

Methodist The Methodist Hospital Research Institute

Houston, TX

LEADING MEDICINE℠

FORTUNE 100 BEST COMPANIES TO WORK FOR 2007

EOE

FACULTY POSITIONS

NEUROSCIENCE FACULTY POSITIONS
Western Washington University
Department of Psychology

The Department of Psychology at Western Washington University (WWU) is seeking candidates for two tenure-track **ASSISTANT PROFESSOR** positions in behavioral neuroscience to begin September 16, 2008. These, together with a third position in the Department of Biology (also advertised in this issue), are part of a state-funded initiative to enhance a new Behavioral Neurosciences program at WWU. The Psychology Department is seeking faculty with expertise in molecular neuroscience or systems neuroanatomy who are working in areas of behavioral neuroscience broadly defined to include perception, attention, learning and memory, and executive function. Successful candidates will be required to maintain an active research program involving undergraduate and M.S. graduate students. Successful candidates will be expected to teach undergraduate and graduate neuroscience courses. Additional teaching may include courses in research methods and statistics. Applicants must have a Ph.D. and postdoctoral experience in neuroscience or a related field, an active research program, evidence of an ability to involve students in research, a publication record commensurate with experience, and evidence of successful teaching. Experience working with diverse students and faculty is desired. To apply, send a hard copy of your curriculum vitae, statements of teaching and research interests, representative publications, evidence of skill as a teacher, and three letters of recommendation to the: **Neuroscience Search Committee, Department of Psychology, Western Washington University, 516 High Street, Bellingham, WA 98225-9089.** Review of applications will begin November 1, 2007. Applications will be accepted and reviewed until the position is filled. For additional details see **website: http://www.acadweb.wwu.edu/hr.** *Affirmative Action/Equal Opportunity Employer.*

ASSISTANT PROFESSOR
Marine Invertebrate Zoology/Benthic Ecology

The Marine Science Program and the Department of Biological Sciences at the University of South Carolina invite applications for a nine-month academic year, tenure-track, Assistant Professor position as primary marine science faculty. A Ph.D. is required prior to appointment. Postdoctoral experience is essential. The Marine Science Program consists of 40 faculty from such Departments as Biology, Geology, and Chemistry. We are looking for an individual with outstanding research and teaching capabilities to complement existing programs in physical, chemical, biological and geological oceanography.

We seek an individual who will contribute to our strengths in estuarine and coastal ocean processes. Our primary area of interest is marine benthic ecology, but we will consider applicants in the areas of zooplankton ecology, invertebrate physiology, and organism/environment interactions. The successful candidate will teach courses on marine organisms and invertebrate zoology and develop an externally funded research program. Applications must include curriculum vitae, statement of research and teaching interests and goals, and at least three references.

Send information to: **Chair, Marine Invertebrate Zoology/Benthic Ecology Search Committee, Department of Biological Sciences, University of South Carolina, Columbia, SC 29208.** Applications should be submitted by December 1, 2007. For more information about the Marine Science Program and the Department of Biological Sciences visit **websites: http://www.msci.sc.edu** and **http://www.biol.sc.edu.** *The University of South Carolina is an Affirmative Action, Equal Opportunity Employer. Women and minorities are encouraged to apply.*

FACULTY POSITIONS

Florida Institute of Technology

ECOLOGIST
Florida Institute of Technology

The Department of Biological Sciences at the Florida Institute of Technology seeks an individual with significant academic accomplishments in ecology. Successful candidates must have a Ph.D. degree in a biological science, demonstrated excellence in research and teaching, and an extramurally funded research program. The area of ecological specialization of the candidate is open, as is the rank of appointment. The successful candidate will be expected to teach undergraduate and graduate courses (toward M.S and Ph.D. degrees) in ecology. For more information please visit **website: http://www.fit.edu/biology.** Applicants should send a letter of application, curriculum vitae, and three letters of recommendation to **e-mail: rvw@fit.edu.** Alternatively, materials may be sent to:

Ecologist Search Committee Chair
(R. van Woesik)
Department of Biological Sciences
Florida Institute of Technology
150 W. University Boulevard
Melbourne, FL 32901 U.S.A.

Review of applications will begin November 1, 2007; the position will commence on August 4, 2008. *Florida Institute of Technology is an Equal Opportunity/Affirmative Action Employer. Women and minorities are encouraged to apply.*

ASSISTANT PROFESSOR
Fungal Evolution, Ecology and/or Systematics

The Department of Ecology and Evolutionary Biology at the University of Tennessee (UT), Knoxville, seeks to fill a tenure-track position in evolution, ecology and/or systematics of fungi at the Assistant Professor level, to start August 1, 2008. Areas of interest include fungal evolutionary and/or ecological patterns and processes. Teaching duties will include participation in both undergraduate and graduate courses with opportunity for development of a course in mycology. This position includes supervision and continued development of the excellent UT fungal herbarium. An earned Ph.D. and refereed publications in a relevant field are required. For more information visit the Department **website: http://eeb.bio.utk.edu** and the herbarium **website: http://tenn.bio.utk.edu/fungus/fungus.html.** Candidates should apply to: **Dr. Randall Small, Department of Ecology and Evolutionary Biology, 569 Dabney Hall, University of Tennessee, Knoxville, TN 37996.** Applicants should send curriculum vitae, statements of research and teaching experience and goals, and arrange for three reference letters to be submitted. Applications will be reviewed beginning 8 October 2007, and will continue until the position is filled.

The University of Tennessee is an Equal Employment Opportunity/Affirmative Action/Title VI/Title IX/Section 504/ADA/ADEA Institution in the provision of its education and employment programs and services. All qualified applicants will receive equal consideration for employment without regard to race, color, national origin, religion, sex, pregnancy, marital status, sexual orientation, age, physical or mental disability, or covered veteran status.

The Department of Biological Sciences at Salisbury University (SU) is accepting applications for two tenure-track positions at the rank of **ASSISTANT PROFESSOR;** one in the area of molecular/cell biology and the other in entomology/general zoology. Starting date for both positions is fall 2008. A Ph.D., evidence of potential for excellence in teaching and research will be required. For further information please see the SU **website: http://www.salisbury.edu/hr/Jobs/default.asp?asearch=faculty.**

FACULTY POSITIONS

FACULTY POSITIONS
Rice University
Biochemistry and Cell Biology
Website: http://www.rice.edu/

Applications are invited for anticipated open-rank faculty positions in broad areas of biological research, with particular emphasis in cell and developmental biology of model organisms, systems biology, and molecular evolution. Applicants using experimental and/or theoretical biological approaches that are interdisciplinary with chemistry, physics, engineering, and computational methods are encouraged to apply. Candidates must have a Ph.D., postdoctoral training, and outstanding potential in research and teaching. Successful candidates are expected to develop and maintain a vigorous research program supported by extramural funding and participate in graduate and undergraduate education. Review of applications will commence November 1, 2007, and continue until the positions are filled. Please send letter of application, curriculum vitae, summary of past research, and statement of future research plans, and arrange for four letters of reference to be sent to:

Dr. J. Braam, Chair
Biochemistry and Cell Biology, MS140
Rice University
P.O. Box 1892
Houston, TX 77251-1892

Rice University is an Equal Opportunity/Affirmative Action Employer; women and minority candidates are especially encouraged to apply.

PROKARYOTIC MICROBIOLOGIST

Tenure-track **ASSISTANT PROFESSOR,** beginning August 2008. Teach microbiology and specialty courses, develop an active research program involving undergraduate and M.S. students, and seek external funding (see **website: http://www.villanova.edu/artsci/biology/micro/** for more information). Ph.D. and postdoctoral experience required. Submit curriculum vitae, research plans, statement of teaching philosophy, and official undergraduate and graduate transcripts, and have three letters of recommendations sent, to: **Chair, Microbiologist Search Committee, Department of Biology, Villanova University, Villanova, PA 19085.** Consideration of applications begins 15 October 2007. Villanova is a Roman Catholic university sponsored by the Augustinian order. *Affirmative Action/Equal Employment Opportunity employer, Villanova seeks a diverse faculty committed to scholarship, service, and especially teaching. We seek colleagues who understand, respect, and contribute to the University's mission and values. We consider diversity to be essential for advancing our Department's educational goals.*

ASSISTANT PROFESSOR
The University of Chicago
Department of Chemistry

The Department of Chemistry of the University of Chicago invites applications from outstanding individuals for the position of Assistant Professor of Chemistry. This search is in the areas broadly defined as inorganic, organic, and physical chemistry. Applications must include curriculum vitae, a list of publications, and a succinct outline of research plans, and be supported by three letters of recommendation. Submit materials by mail addressed, as appropriate, to: **Inorganic Search Committee, Organic Search Committee, or Physical Search Committee, Department of Chemistry, Office of the Chairman (Ghj 222), The University of Chicago, 5735 S. Ellis Avenue, Chicago, IL 60637.** Review of completed applications will begin October 1, 2007; to ensure full consideration, all material should be submitted by that date. *University of Chicago is an Affirmative Action/Equal Opportunity Employer.*

ASSISTANT PROFESSOR
DEPARTMENT OF GENETICS
HARVARD MEDICAL SCHOOL

The Department of Genetics invites applicants for the tenure-track position of Assistant Professor. We are searching for individuals with a strong potential for imaginative research in any area of modern genetic or genomic analysis. This position offers significant scholarly and scientific resources as well as the opportunity to teach graduate and medical students.

For further information about our Department, please see our Web Page:

http://genetics.med.harvard.edu

Applicants should submit electronic copies of curriculum vitae, bibliography, a brief description of research accomplishments and future research interests (limit to 500 words) by **October 31, 2007**, and ask three references to provide letters of recommendation. These materials should be sent to the following email address:

faculty_search@genetics.med.harvard.edu

Harvard University is an Equal Opportunity/Affirmative Action Employer and encourages the applications of qualified women and minorities.

Huntsman Cancer Institute
University of Utah

Huntsman Cancer Institute and academic departments at the University of Utah are recruiting tenure-track scientists to establish laboratory-based programs in cancer mechanisms, tumorigenesis models, and translational research. Mechanism topics might include cancer genetics, signal transduction, cell growth and death, developmental mechanisms, regulation of gene expression, DNA repair, and oncogene/tumor suppressor function. Translational research topics might include molecular diagnostics, chemoprevention, and tumor models. Candidates may hold MD, PhD, or MD/PhD degrees; assistant or associate professor rank is most desirable, but senior-level appointments will be considered. Candidates will complement these areas of interest and strength: melanoma (cancer genetics, apoptosis regulation, melanocyte biology, chemoprevention, and drug development); gastrointestinal (APC/wnt signaling, cancer genetics, and colon and pancreatic cancer models); pediatric (sarcoma, leukemia, and neuro-oncology); gynecological; and thoracic cancers. Appointments will be made in appropriate departments, including Oncological Sciences, Pediatrics, Dermatology, Obstetrics & Gynecology, and Surgery.

Huntsman Cancer Institute is an NCI-designated cancer center with shared resources that support imaging, molecular, and biochemical analyses as well as genetics research in human populations and model systems. Utah genealogical records linked to SEER cancer registry data and University of Utah Hospital medical records provide a unique research resource. Visit **www.huntsmancancer.org** and **www.hsc.utah.edu** for more information.

Submit a curriculum vitae and a description of research interests and accomplishments with three letters of recommendation by November 16, 2007: **Huntsman Cancer Institute, University of Utah, Attn: Recruitment Office, 2000 Circle of Hope, Salt Lake City, UT 84112-5550** or e-mail **hci.recruitment@hci.utah.edu**. (Applications accepted until positions filled.) *Equal Opportunity/ Affirmative Action employers. Women, minorities, and international candidates encouraged to apply.*

Department of Communication
College of Agriculture and Life Sciences

Located in Ithaca, N.Y., Cornell University is a bold, innovative, inclusive and dynamic teaching and research university where staff, faculty, and students alike are challenged to make an enduring contribution to the betterment of humanity.

The Department of Communication at Cornell University invites applicants for **two tenure track, open rank professorial** faculty positions appointment starting July 1, 2008. At least one of the positions will be filled at the rank of Assistant Professor. We encourage qualified applicants of any rank to apply for either position.

SCIENCE, ENVIRONMENT, AND/OR RISK COMMUNICATION: We seek a colleague to conduct research and teach in the area of science, environment, and/or health-risk communication. We welcome innovative and imaginative scholars who approach the study of science, environment, and/or health-risk communication from psychological, sociological, or institutional vantage points using qualitative or quantitative methods. The science, environment, and risk area constitutes one of the Department's core strengths; applicants whose work contributes to other core strengths in communication and information technology and in media studies are particularly encouraged to apply. All materials should be sent to **Dr. Bruce Lewenstein, Department of Communication, 321 Kennedy Hall, Cornell University, Ithaca, NY 14853. For additional information, e-mail Dr. Lewenstein (b.lewenstein@cornell.edu) or telephone 607.255.8310.**

COMMUNICATION AND INFORMATION TECHNOLOGY: We seek a colleague to conduct research and to teach in the area of Communication and Information Technology, with an emphasis in one or more of the following: 1) Human-Computer Interaction, 2) Computer-Mediated Communication, 3) IT in organizations, and 4) Technology and Society. The communication and information technology area constitutes one of the Department's core strengths; applicants whose work contributes to other core strengths in media studies and in science, environment and risk are particularly encouraged to apply. All materials should be sent to **Dr. Jeff Hancock, Department of Communication, 320 Kennedy Hall, Cornell University, Ithaca, NY 14853. For additional information, e-mail Dr. Hancock (jth34@cornell.edu) or telephone 607.255.4452.**

Successful candidates for either position will have a Ph.D. in Communication or closely aligned field and have (or show promise of developing) a national and international reputation doing theory-based empirical research. We seek innovative scholars of social science who will develop a research program connected to college and university priorities in applied social science, information science, the new life sciences, environmental issues, and/or public outreach. In the Department of Communication we focus on a number of subfields including social psychology of communication; language and communication; science, risk, environment, and health communication; human-computer interaction; media communication and society; and organizational communication. Both positions will involve 50% research and 50% teaching responsibilities; publishing in peer-reviewed literature in relevant fields is expected. In addition, successful candidates are expected to secure external research funding. Communication faculty teach two to three undergraduate and/or graduate courses per academic year, and advise students in the Department's B.S., M.S., and Ph.D. programs.

Cornell offers a highly competitive salary and benefits package. Support for start-up research costs will be available. Women and minorities are especially encouraged to apply. Applications will be reviewed beginning October 15, 2007 until candidates are selected. For more information about the Department of Communication, please visit our website: **http://www.comm.cornell.edu**.

Application: Send letter of application addressing position qualifications and goals, vita, official academic transcripts, writing sample, names and contact information of three references. Please also have each reference submit a letter of recommendation.

Cornell University

Cornell University is an Affirmative Action/ Equal Opportunity Employer and Educator.

http://chronicle.com/jobs/profiles/2377.htm

RUTH C. and ANDREW G. COWLES PROFESSOR of BIOLOGY-NEUROBIOLOGY
Trinity University, San Antonio, Texas

The Biology Department of Trinity University seeks a broadly trained **NEUROBIOLOGIST** for the Ruth C. and Andrew G. Cowles Professor of Biology. We are searching for a candidate with an established record of scholarship and teaching commensurate with an endowed professorship. This position provides a competitive salary and designated funds for research support. The successful candidate will teach neurobiology, contribute to the biology curriculum, advise undergraduate students, and provide leadership for a growing interdisciplinary major in neuroscience. The candidate is expected to establish an active research program that involves undergraduates. Applicants should send curriculum vitae, statement of teaching philosophy, summary of research interests, and contact information for three references to: **Prof. David O. Ribble, Chair, Department of Biology, Trinity University, One Trinity Place, San Antonio, TX 78212,** or e-mail materials to **e-mail: dribble@trinity.edu.** Trinity University is a private, independent, primarily undergraduate institution that emphasizes quality teaching and active research. Additional information can be found at **website: http://www.trinity.edu/departments/biology.** We will begin reviewing candidates 22 October 2007. *Women and minority candidates are strongly encouraged to apply. Trinity University is an Equal Opportunity Employer.*

The Department of Biological Sciences at Le Moyne College seeks two tenure-track **ASSISTANT PROFESSORS** to begin August 2008. Responsibilities for position one include teaching courses in genetics and bioinformatics. Responsibilities for position two include teaching in and eventually coordinating a multisection anatomy and physiology course. Additional responsibilities for both positions include teaching upper-level courses in applicant's area of expertise, advising biology majors, and implementing a research program that encourages undergraduate participation; ability to teach in introductory or nonmajors courses essential. Ph.D. required at time of appointment; undergraduate teaching experience preferred. A letter of application (indicating position sought) with curriculum vitae, transcripts, and separate statements of teaching philosophy and research interests should be submitted electronically to **e-mail: lemoynehr@lemoyne.edu** with a subject line of either BIO-Genetics, or BIO-Physiology. Additionally, please arrange to have three letters of recommendation sent electronically to this address with the appropriate position subject line. Review of applications will begin October 5, 2007, and continue until the position is filled. Visit our webpage at **website: http://www.lemoyne.edu.**

Le Moyne College is an Equal Opportunity Employer and encourages women, persons of color, and Jesuits to apply for employment.

ASSISTANT PROFESSOR

The Department of Biochemistry and Molecular Biology, Brody School of Medicine at East Carolina University is seeking applications for a tenure-track position as an Assistant Professor. Preference will be given to candidates having basic research expertise in areas related to obesity and diabetes. The candidate will be expected to actively participate in the teaching mission of the Department and develop a successful externally funded research program. See **website: https://ecu.peopleadmin.com/applicants/Central?quickFind=56146** for full ad and electronic application. *East Carolina University is an Equal Opportunity/Affirmative Action University that accommodates individuals with disabilities. Individuals requesting accommodation under the Americans with Disabilities Act should contact the Department for Disability Support Services at* ***telephone: 252-737-1016*** *(voice/TTY). Proper documentation of identity and employability is required at the time of employment.*

LEHIGH UNIVERSITY

ASSISTANT PROFESSOR
Microbial Genomics

Lehigh University's Department of Biological Sciences **(website: http://www.lehigh.edu/~inbios)** invites applications for a tenure-track Assistant Professor position in microbial genomics to begin in fall 2008. Applicants with expertise in evolutionary genomics, functional genetics, or systems biology as applied to microbes are particularly encouraged to apply. The successful candidate will have the potential or demonstrated ability to generate extramural funding and a commitment to instructional excellence at the undergraduate and graduate levels. The College of Arts and Sciences at Lehigh is especially interested in qualified candidates who can contribute, through their research, teaching, and/or service, to the diversity and excellence of the academic community.

Applications should be directed to: **Prof. L. Cassimeris, Chair, Microbial Genomics Search Committee. E-mail: inbios@lehigh.edu.** Send curriculum vitae, representative publications, description of research and teaching interests, and four letters of reference to the **Search Committee Chair** electronically or to: **Department of Biological Sciences, 111 Research Drive, Lehigh University, Bethlehem, PA 18015.** Deadline for submission is December 1, 2007.

Lehigh University is an Equal Opportunity Affirmative Action Employer. Lehigh University provides comprehensive benefits including partner benefits.

DEPARTMENT of ECOLOGY and EVOLUTIONARY BIOLOGY
University of Connecticut

LANDSCAPE to GLOBAL-SCALE ECOLOGIST. The Department of Ecology and Evolutionary Biology at the University of Connecticut **(website: http://www.eeb.uconn.edu)** announces a tenure-track **ASSISTANT PROFESSOR** position for an **AQUATIC or TERRESTRIAL ECOLOGIST** working at landscape to global scales. Possible research areas include, but are not limited to: patch dynamics; metapopulation, metacommunity, or landscape ecology; phylogeography, biogeography, macroecology, species distribution modeling, paleoecology, or global change ecology. Candidates whose research and teaching interests integrate aspects of the Department's core strengths in ecology, conservation, evolution, and systematics, in the wider context of the campus community of environmental scientists and engineers will be favored. Qualifications: Candidates must have a Ph.D.; postdoctoral experience is desirable. A letter of application, statements of research and teaching interests, curriculum vitae, and three letters of reference should be addressed to: **Dr. Robert K. Colwell, Department of Ecology and Evolutionary Biology, Unit 3043, University of Connecticut, Storrs, CT 06269-3043.** Electronic applications (send to **e-mail: kathleen.tebo@uconn.edu)** are strongly preferred. Review of applications will begin November 1, 2007, and continue until the position is filled. *At the University of Connecticut, our drive to excel includes a commitment to building a culturally diverse community. We encourage members of underrepresented groups, including minorities, women, and people with disabilities, to apply.*

ASSISTANT PROFESSOR. Tenure-track faculty position in Department of Chemical Engineering and Materials Science at University of California, Davis, in experimental thermodynamics of materials. Ph.D. in materials science, chemical engineering, chemistry, or related discipline required. Apply at **website: http://www.chms.ucdavis.edu/employment/.** Position open until filled; but to assure full consideration, submit applications no later than October 30, 2007. Start date July 1, 2008. *UC Davis is an Affirmative Action/Equal Opportunity Employer, and is dedicated to recruiting a diverse faculty community.*

CONDENSED MATTER/BIO SEARCH

The Physics Department, the James Franck Institute, and the Institute for Biophysical Dynamics at the University of Chicago invite applications for a tenure-track faculty appointment in the areas of experimental biophysics and experimental condensed matter physics. The appointment will start in the fall of 2008. The successful candidate must have a doctoral degree in physics or related fields, and is expected to establish an independent research program while effectively contributing to the Physics Department's undergraduate and graduate teaching programs.

The appointment is expected to be at the **ASSISTANT PROFESSOR** level. Appointment at the level of **ASSOCIATE PROFESSOR or FULL PROFESSOR** is possible for exceptionally well qualified candidates. Applicants should send curriculum vitae, a list of publications, a brief research statement, and arrange to have at least three reference letters sent to:

Professor Heinrich Jaeger, Director
James Franck Institute, CIS E 145
The University of Chicago
929 E. 57th Street
Chicago, IL 60637

E-mail inquiries should be sent to **Ms. Rosemary Garrison** at **e-mail: rg-garrison@uchicago.edu.** Review of applications will start in the fall of 2007, and will continue until the position is filled. To ensure full consideration, applications should be received no later than November 1, 2007. *The University of Chicago is an Equal Opportunity, Affirmative Action Employer.*

TENURE-TRACK BIOLOGIST

The University of the South seeks to hire a tenure-track **ASSISTANT PROFESSOR** of Biology. The successful candidate will teach upper-division undergraduate courses in genomics, molecular genetics or/and evolution, participate in the Department's introductory biology classes, and maintain an active research program with opportunities for undergraduate involvement. Candidates should be enthusiastic about developing a teaching and research program in the context of the liberal arts tradition in education. The College of Liberal Arts and Sciences at the University has an undergraduate enrollment of about 1,400 and is located on a biologically diverse 10,000-acre campus on Tennessee's Cumberland Plateau. Review of applicants will begin on October 8, 2007, but applications will be accepted until a suitable candidate is found. Send a letter of application, curriculum vitae, statements of teaching and research interests, transcripts, and three letters of reference to: **Teresa Smith, Personnel Services, 735 University Avenue, The University of the South, Sewanee, TN 37383.** Submissions via e-mail are preferred; send to **e-mail: tersmith@sewanee.edu.** More information about the position can be found at **website: http://www.sewanee.edu/biology/search.html.** *The University of the South is an Equal Opportunity Employer. Minorities and women are encouraged to apply.*

VERTEBRATE BIOLOGY FACULTY POSITION. The Department of Biology at Clark University, Worcester, Massachusetts **(website: http://www.clarku.edu/departments/biology/)** invites applications for a tenure-track appointment at the rank of **ASSISTANT PROFESSOR,** to begin fall 2008. The successful candidate will be expected to develop an externally funded research program in any area of vertebrate biology involving Ph.D. and undergraduate students. The candidate will teach human and comparative anatomy courses, and other appropriate courses. Applicants should submit curriculum vitae, summary of research and teaching interests, and three publications. Three letters of reference should be received by the **Search Committee** prior to October 15, 2007, for full consideration **(e-mail: vert@clarku.edu). Please see website: https://www.clarku.edu/offices/hr/jobsdb.cfm?id=376&viewjob=1&grouping=F** for full position description. Inquiries may be directed to **e-mail: sfoster@clarku.edu.** *Affirmative Action/Equal Opportunity Employer. Minorities and women are especially encouraged to apply.*

FACULTY POSITIONS

ASSISTANT PROFESSOR, Chemistry/Biochemistry. The Department of Chemical Sciences, Bridgewater State College, Bridgewater, Massachusetts, invites applications for a new full-time, tenure-track Assistant Professorship beginning in September 2008. The successful candidate will have a strong commitment to undergraduate teaching (especially biochemistry and introductory chemistry) and in developing a research program appropriate to an undergraduate setting (see **website: http://www.bridgew.edu/ATP/** for a description of our undergraduate research program).

A Ph.D. and postdoctoral experience in biochemistry or a related area are required, as are excellent oral and written communication skills. Prior college teaching experience is preferred, as are candidates with a background in one or more of the following areas: toxicology, analytical biochemistry, computational biochemistry, or biophysical chemistry.

To apply: Please visit our employment **website: http://www.bridgew.edu/HR/JobList/** and submit electronically a letter of application, curriculum vitae, and statements of teaching philosophy and research plans. In addition, please mail official graduate transcripts and arrange to have three letters of recommendation sent to: **Chair, Faculty Search Committee, Department of Chemical Sciences, Bridgewater State College, Bridgewater, MA 02325.** Review of complete applications will begin on October 19, 2007, and continue until the position is filled.

Bridgewater State College is an Affirmative Action/Equal Opportunity Employer that actively seeks to increase the diversity of its work force.

The Department of Chemistry and Biochemistry at the University of Maryland, Baltimore County (UMBC) invites applications for tenure-track faculty positions in the areas of biochemistry, physical chemistry, and organic chemistry (including biophysical and bioorganic) to begin August 2008. All positions are anticipated to be filled at the **ASSISTANT PROFESSOR** level, although highly qualified applicants will be considered for appointment at a higher level. Successful candidates are expected to establish strong research programs and teach at both the undergraduate and graduate levels. Applicants should submit curriculum vitae, description of research plans, a statement of teaching philosophy, and arrange for three letters of recommendation to be sent to: **Dr. Lisa Kelly, Chair, Faculty Search Committee Department of Chemistry and Biochemistry, University of Maryland, Baltimore County, 1000 Hilltop Circle, Baltimore, MD 21250.** Electronic submissions can be made to **e-mail: chemsearch@umbc.edu.** *UMBC is an Equal Opportunity/Affirmative Action Employer; and applications from women, minorities and individuals with disabilities are especially encouraged. Applications will be received until positions are filled.*

UNIVERSITY of VIRGINIA
Department of Chemistry

We invite applications for a tenure-track **ASSISTANT PROFESSOR** in the field of chemical biology, beginning August 25, 2008. Selection criteria will include a Ph.D. in a related field, a strong record of innovative research, the potential for establishing an active and highly visible research program, and an interest and commitment to teaching excellence. Applicants with research interests in chemical genetics and functional proteomics or in emerging areas of bioanalytical, biophysical, and biomaterials chemistry are particularly encouraged. Search Committee review of applications will begin October 31, 2007, but applications will continue to be accepted for consideration until the position is filled. Applicants should send curriculum vitae, a brief description of future research plans, and arrange for three letters of recommendation to be sent to: **Chair, Faculty Search Committee, Department of Chemistry, University of Virginia, P.O. Box 400319, Charlottesville, VA 22904-4319.** *The University of Virginia is an Equal Opportunity/Affirmative Action Employer and is strongly committed to building diversity within its community.*

FACULTY POSITIONS

ALMA COLLEGE
ONLY ONE ALMA.

MOLECULAR BIOLOGY. ASSISTANT PROFESSOR, full-time, tenure-track position in biology. A Ph.D. is required and position starts fall term 2008. The Biology Department seeks an individual with demonstrable skills in, and commitment to, undergraduate teaching and research. Teaching responsibilities will include general genetics plus laboratories, a nonmajor introductory biology course, seminar, and an elective upper-level course attractive to pre professionals. Areas of specialty could include health-based genetics, histology, endocrinology, or molecular pathology. Interest in interdisciplinary applications particularly welcome. Review of applications begins October 24, 2007. Applicants should provide curriculum vitae, a statement of teaching and research interests and expertise, and arrange for official graduate transcripts and three letters of reference to be sent to: **Dr. David Clark, Department of Biology, Alma College, 614 W. Superior Street, Alma, MI 48801; telephone: 989-463-7058.** For more information, visit our **website: http:// www.alma.edu/academics/biology.** *Alma College is an Affirmative Action/Equal Opportunity Employer.*

TENURE-TRACK POSITION in BIOCHEMISTRY

Applications are invited for a tenure-track position in biochemistry in Macalester College's Department of Biology at the **ASSISTANT PROFESSOR** rank beginning fall 2008. We seek applicants who are committed to excellence in teaching at the undergraduate level and who are dedicated to developing an active research program that engages students in research. More details on this position are available at **website: http://www.macalester.edu/provost/positions/.**

To apply for the position, send a letter, curriculum vitae, statements of teaching philosophy and research plans, and three letters of reference to: **Professor Lin Aanonsen, Chair, Department of Biology, Macalester College, St. Paul, MN 55105.** Applications received by October 15, 2007, will receive first consideration. Macalester College is a selective, private liberal arts college in the Minneapolis-St. Paul metropolitan area. The College prides itself on providing support for excellence in teaching and in faculty scholarship. *As an Equal Opportunity Employer supportive of affirmative efforts to achieve diversity among its faculty, Macalester College strongly encourages applications from women and members of underrepresented minority groups. We are especially interested in candidates committed to working with students of diverse backgrounds.*

ASSISTANT PROFESSOR
Plant Biology/Botany

The Biological Sciences Department of the University of Wisconsin, Parkside, seeks a **PLANT BIOLOGIST or BOTANIST** to fill a tenure-track Assistant Professor (nine-month) position to begin August 2008. Applicants must have a Ph.D. and postdoctoral experience. Applications received by November 1, 2007, are ensured full consideration; position is open until filled. Send a letter of application, vitae, reprints, description of research interests, a statement of teaching philosophy and three letters of reference to: **Search Committee, Department of Biological Sciences, University of Wisconsin-Parkside, 900 Wood Road, P.O. Box 2000, Kenosha, WI 53141; telephone: 262-595-2744.** A full announcement can be obtained online at **website: http://www.uwp.edu,** keyword jobs, then follow Unclassified Positions link. *UW, Parkside, is an Affirmative Action/Equal Employment Opportunity Employer. Persons with Disabilities, Minorities, Veterans, Women.*

FACULTY POSITIONS

ASSISTANT PROFESSOR
(Molecular Microbiology/Immunology)

The Department of Biological Sciences at Purdue University Calumet invites applications for a tenure-track position to begin in August 2008. A Ph.D. degree and excellent verbal/written communication skills are required. Postdoctoral experience is preferred. Responsibilities will include (1) teaching undergraduate and graduate courses in microbiology, immunology, upper division courses in areas of expertise and potentially introductory biology, (2) establishing a vigorous extramurally funded research program, involving graduate/undergraduate students, that will complement and enhance current departmental strengths in molecular biology and biotechnology, and (3) service to the University. Purdue University Calumet, the Chicago-area campus of the Purdue University system, is an M.S. Comprehensive University with over 9,400 students, of which approximately 425 undergraduate majors and 30 graduate students are enrolled in the Department of Biological Sciences **(website: http://www.calumet.purdue.edu/biology/).** Review of applications will begin November 2007 and continue until the position is filled. Inquiries or letters of application stating teaching philosophy and research interests, curriculum vitae, copies of graduate/undergraduate transcripts, and three original letters of recommendation with contact information should be sent to: **Dr. W-T Evert Ting, Chair of Search Committee, Department of Biological Sciences, Purdue University Calumet, 2200 169th Street, Hammond, IN 46323-2094 (e-mail: biosearch@calumet.purdue.edu).** *Purdue University Calumet is an Equal Access/Equal Opportunity/Affirmative Action Employer.*

ASSISTANT PROFESSOR, PLANT BIOLOGY

The Department of Biological Sciences, California State University, Los Angeles, seeks to fill a Tenure-Track Position in plant biology beginning fall 2008. A Ph.D. in biology, botany, or related field is required, with a minimum of one year of postdoctoral experience preferred. The candidate is expected to teach undergraduate and graduate courses, participate in program development, and establish an externally funded research program involving undergraduate and Master's students. The candidate is also expected to participate in University service, and to provide academic advisement to students. Submit curriculum vitae, research plans, statement of teaching philosophy, and three letters of reference to: **Search Committee Chair - Plant Biologist, Department of Biological Sciences, California State University, Los Angeles, 5151 State University Drive, Los Angeles, CA 90032 (e-mail: plapolt@exchange.calstatela.edu).** Review of completed applications will begin November 1, 2007, and may continue until position is filled. *EO/Title IX/ADA Employer. Qualified women and minorities are encouraged to apply.*

FACULTY POSITION at the UNIVERSITY of PUERTO RICO

The Department of Biology of the University of Puerto Rico at Rio Piedras **(website: http://biology.uprrp.edu)** invites applications for a tenure-track position in bioinformatics. Candidates with expertise in evolution, proteomics/genomics, and physiological systems are preferred. Applicants must hold a Ph.D. or equivalent and have postdoctoral experience. Candidates are expected to develop active research programs and to teach at the graduate and undergraduate levels. Interested persons should send resume, a statement of current and future research and teaching goals, representative publications and three letters of reference to: **Dr. James Ackerman, P.O. Box 23360, UPR Station, San Juan, PR 00931-3360** or **e-mail: ackerman.upr@gmail.com.** Applications will be reviewed from October 1, 2007, until the position is filled. *University of Puerto Rico is an Equal Opportunity Employer.*

FACULTY POSITION
SEALY CENTER FOR CANCER CELL BIOLOGY AND DEPARTMENT OF MICROBIOLOGY AND IMMUNOLOGY THE UNIVERSITY OF TEXAS MEDICAL BRANCH (UTMB)

The Department of Microbiology and Immunology and the Sealy Center of Cancer Cell Biology at UTMB are seeking an experienced researcher for a tenure track position at the Assistant or Associate Professor level. Candidates are expected to engage in research and teaching activities in the Department and in campus-wide programs in cancer and immunology. The candidate should have an MD, DVM, PhD, or MD/PhD degree and a background that includes the potential to build a strong extramurally funded research program.

Preferential consideration will be given to those with a research background in the areas of tumor inflammation, tumor immunology, tumor microenvironment and tumor cell biology. The successful candidate will have demonstrated academic scholarship in the form of publications in major peer-reviewed journals and a record of continued extramural research funding or the potential to establish a funded program.

Recruited faculty will be provided with generous start-up packages, competitive compensation and benefits, modern laboratory space within the center, and access to state-of-the-art core facilities. Diversity is a key UTMB core value, and actively sought in our applicant pools, including, ethnic, cultural, gender and research interests. The city of Galveston, a popular tourist destination that includes beaches, museums, historical sights, four cruise lines, and excellent restaurants, is 45 minutes away from Houston, the nation's fourth largest city. The University of Texas Medical Branch (UTMB), is the oldest medical school in the state and has a research base that rivals most public universities in the country. Its collaboration between departments in both conducting research and teaching is one of the strengths of the institution.

Applicants for an assistant professor position should have at least three years of post-doctoral or equivalent experience and a strong publication record. Candidates for an associate professor position should have established, funded research programs and a strong publication record. Please send electronic copies of a curriculum vitae, statement of research interests and goals, and the names of four references to: **B. Mark Evers, M.D. Sealy Center for Cancer Cell Biology, The University of Texas Medical Branch, Galveston, Texas, http://www.utmb.edu/scccb/** email: **reply.scccb@utmb.edu.**

UTMB is an Equal Opportunity, Affirmative Action Institution that proudly values diversity. Candidates of all backgrounds are encouraged to apply.

Yale University
School of Medicine

FACULTY POSITION AT THE JUNIOR OR SENIOR LEVEL

DEPARTMENT OF CELLULAR AND MOLECULAR PHYSIOLOGY

The Department of Cellular and Molecular Physiology seeks applicants for a faculty position at the junior or senior level. Candidates must hold a Ph.D., M.D., or equivalent degree. The candidate's research interest should be in the general area of cellular and molecular physiology with particular emphasis in integrative or translational research and in genetic model systems. Outstanding candidates working in other areas of cellular, molecular, and systems physiology are also encouraged to apply. Excellent opportunities are available for collaborative research, as well as for graduate and medical student teaching.

Applicants should include a curriculum vitae, a statement of research interests and goals, and three letters of reference. Applications should be emailed to leisa.strohmaier@yale.edu in PDF format or sent to:

Dr. Steven C. Hebert, Chair
Department of Cellular and Molecular Physiology
Yale University School of Medicine
333 Cedar Street
P.O. Box 208026
New Haven, CT 06510

Application Deadline: **November 1, 2007**

Yale University is an Affirmative Action/Equal Opportunity Employer.

Department of Biology
University of Nevada, Reno

Ecologists (2) and Developmental Biologist

The Biology Department at the University of Nevada, Reno (UNR), seeks two **ECOLOGISTS** and one **DEVELOPMENTAL BIOLOGIST** for tenure track positions to start July 2008. The department has targeted EECB (ecology, evolution, and conservation biology) and developmental biology as its two strategic foci for growth. The department's EECB faculty have well established excellence in conservation biology, conservation genetics, behavioral ecology, and evolutionary ecology. The ecology positions are: (1) **ASSISTANT/ASSOCIATE PROFESSOR** with strong interests in conservation biology and (2) **ASSISTANT PROFESSOR** with area of specialization open. Nevada remains one of the least studied parts of North America, and there are many ecological and conservation challenges in the Mojave Desert, the Great Basin, and nearby California. Diverse funding opportunities exist for research on these challenges. Our five developmental biologists form the core of an emerging area of excellence that is well funded by NIH and NSF. For the **ASSISTANT PROFESSOR** of developmental biology position, research interests can be in developmental biology or in another complementary area of cell or molecular biology. UNR has outstanding core facilities for genomic and proteomic research. The successful candidates will be provided with competitive start-up packages and will be expected to maintain nationally recognized, extramurally funded research programs. The Department has ~ 620 majors, ~ 45 MS and PhD students, ~ 24 state-funded faculty, and averages ~ $4 million/yr in extramural awards. Reno sits on the eastern flank of the Sierra Nevada in close proximity to desert and montane field sites and to Lake Tahoe. Reno was recently rated one of the best small cities in the US for overall quality of life. Applicants should send application letter, curriculum vitae, statement of research plans, and contact information for 3 references electronically at website: **http://www.unrsearch.com**. Please specify the position for which you are applying. For complete position announcement and requirements, visit website: **http://jobs.unr.edu**. Applications received by **October 15, 2007** will receive full consideration.

Equal Employment Opportunity/Affirmative Action. Women and underrepresented groups are encouraged to apply.

FACULTY POSITIONS

FACULTY of HEALTH SCIENCES
Queen's University
Kingston, Ontario - Canada
Department of Anatomy and Cell Biology

Applications are invited for a tenure-track appointment at the rank of **ASSISTANT PROFESSOR.** A Ph.D. and/or M.D. or D.D.S. or D.V.M. degree and a minimum of two years of postdoctoral experience are required. This advertisement is directed to outstanding candidates who have established or planned research programs with a strong molecular and cellular background in developmental biology. The successful candidate will teach in one or more of the following areas: embryology, human gross anatomy, histology/cell biology, neuroanatomy.

Candidates are to forward a letter of application together with curriculum vitae and the names and contact information of three references to: **Dr. Charles Graham, Chair, Appointment Committee, Department of Anatomy and Cell Biology, Faculty of Health Sciences, Queen's University, Kingston, Ontario K7L 3N6.** Review of applications will commence on November 1, 2007, and continue until the position is filled. Letters of reference will be requested only from those candidates who are shortlisted.

The University invites applications from all qualified individuals. Queen's University is committed to employment equity and diversity in the workplace and welcomes applications from women, visible minorities, aboriginal people, persons with disabilities, and persons of any sexual orientation or gender identity. Academic staff at Queen's are governed by a collective agreement between the Queen's University faculty and the University which is posted at ***website: http://www.queensu.ca/qufa.*** *All qualified candidates are encouraged to apply, however, Canadian citizens and permanent residents will be given priority.*

ASSISTANT PROFESSOR in BIOLOGY

The Department of Biology at the University of North Florida invites applications for a tenure-track Assistant Professor in toxicology beginning August 2008. Candidates must have a Ph.D. in the biological sciences or an appropriate related field, a commitment to undergraduate education, and the potential to establish an independent externally funded research program appropriate for student participation. Teaching will include undergraduate and Master's level courses in the area of specialty and shared responsibility for introductory courses. The Department is growing rapidly and has a new Flagship Program in Coastal Biology. For more information visit **website: http://www.unf.edu/coas/biology.** Candidates must complete an online application **(website: http://www.unfjobs.org)** and submit a cover letter, curriculum vitae, transcripts, concise statements of research interests and teaching philosophy, and three letters of reference to: **Dr. Judith D. Ochrietor, Search Committee Chair, Department of Biology, University of North Florida, 1 UNF Drive, Jacksonville, Florida 32224-2660,** by postmark deadline November 5, 2007. *UNF is an Equal Opportunity/Equal Access/Affirmative Action Institution.*

MOLECULAR MICROBIOGIST/ MOLECULAR CELL BIOLOGIST

The Sonoma State University Biology Department is seeking a dynamic teacher-scholar for a tenure-track **ASSISTANT PROFESSOR** position starting fall 2008. Research specialty is open, but we are especially interested in individuals with postdoctoral training who investigate microbiological, cellular, or molecular processes of biomedical relevance. The successful candidate will be expected to maintain an externally funded research program involving both undergraduate and graduate students and teach in his/her areas of expertise. Review of completed applications will begin October 21, 2007. See full job announcement at our **website: http://www.sonoma.edu/aa/fa/.**

FACULTY POSITIONS

Penn
University of Pennsylvania

UNIVERSITY of PENNSYLVANIA
Department of Chemistry
Faculty Position in Chemistry

The Department of Chemistry at the University of Pennsylvania plans to make a tenure-track appointment in chemistry at the **ASSISTANT PROFESSOR** level. The appointment will be in the area of biological chemistry/chemical biology. Applicants should send their curriculum vitae, a list of publications, a description of proposed research and three reference letters to: **Faculty Search Committee, Department of Chemistry, University of Pennsylvania, Philadelphia, PA 19104-6323.** Letters of reference can also be sent to **e-mail: search@chem.upenn.edu.** Applicants must also complete a profile at **website: https://fusion.sas.upenn.edu/faculty/pos/chem/bio.htm.** Review of applications will begin on October 1, 2007, and will continue until the position is filled. *The University of Pennsylvania is an Equal Opportunity/Affirmative Action Employer. Minority and women applicants are especially encouraged to apply.*

BIOCHEMISTRY FACULTY POST

Bucknell University seeks outstanding candidates for an entry-level, tenure-track position at the rank of **ASSISTANT PROFESSOR** scheduled to begin in August 2008. The successful applicant will teach biochemistry, lecture, and laboratory, and will also teach introductory organic chemistry, general chemistry, or introductory inorganic chemistry, depending on background and interests. The successful candidate will also have the opportunity to develop advanced course(s) within his/her area(s) of expertise. The development of a vigorous research program in some area of biochemistry (including bioorganic, bioinorganic, and chemical biology) is expected, and this research program will involve undergraduate and Master's students. Ph.D. required, postdoctoral experience preferred. Applications can be submitted at **website: http://www.bucknell.edu/jobs,** and should include curriculum vitae, a detailed description of research interests and plans, and a statement of teaching interests. Additionally, three letters of recommendation are to be sent directly to: **Professor Timothy G. Strein, Chair of the Biochemistry Search Committee, Department of Chemistry, Bucknell University, Lewisburg, PA 17837 (e-mail: strein@bucknell.edu).** Review of applications will begin on October 5, 2007. *Bucknell University encourages applications from women and members of minority groups (Equal Employment Opportunity/Affirmative Action).*

ASSISTANT PROFESSOR
Biological Chemistry
The David Geffen School of Medicine at UCLA

The Department of Biological Chemistry is seeking applications for an Assistant Professor, tenure track, in any area of biochemistry or molecular, cell, and developmental biology. More advanced candidates may be considered under special circumstances. The new faculty member will be expected to develop a strong and creative research program and to contribute to departmental teaching.

Candidate selection will begin December 15, 2007, and continue until the position is filled. Applicants should send curriculum vitae, a summary of research interests, and arrange for three letters of reference to be sent to:

Peter Edwards, Ph.D.
Chair, Search Committee
c/o Judy Alvarez
UCLA Biological Chemistry
P.O. Box 951737, 310 BSRB
Los Angeles, CA 90095-1737

The University of California is an Affirmative Action/Equal Opportunity Employer.

FACULTY POSITIONS

DEPARTMENT of CHEMISTRY
Inorganic Chemistry

The Department of Chemistry in the College of Arts and Sciences at American University seeks a full-time tenure-track faculty member at the rank of **ASSISTANT PROFESSOR** for academic year 2008-2009. The successful candidate must have a Ph.D. in chemistry and be able to show evidence of strong teaching skills. Primary teaching responsibilities include general chemistry and liberal arts chemistry. Applicants are expected to maintain a strong research record. Other responsibilities also include supervising graduate and undergraduate research students and mentoring both undergraduate and graduate students. To apply, submit a letter of application, curriculum vitae, a statement of research interests, and a research plan, and arrange to have three letters of reference sent directly from individuals who are able to comment on the applicant's teaching and research skills to: **Dr. James E. Girard, Department of Chemistry, American University, 4400 Massachusetts Avenue N.W., Washington, DC 20016-8104; e-mail: jgirard@american.edu; fax: 202-885-1752.** E-mail submissions are encouraged. American University is seeking highly dedicated teachers and scholars who are deeply committed to interdisciplinary learning, the application of new technologies in teaching and scholarship, and to the preparation of students for life in a diverse and rapidly changing global society. *Women and minority candidates are strongly encouraged to apply. American University is an Affirmative Action/Equal Opportunity Employer.*

SENIOR FACULTY POSITION
Temple University
Department of Chemistry

The Department of Chemistry at Temple University invites nominations and applications for a faculty position at the **FULL/ASSOCIATE PROFESSOR** level in any area of chemistry. Applicants are expected to have established research programs of high quality, supported by substantial externally funded peer-reviewed research grants and demonstrated significant teaching accomplishments. Salaries are highly competitive and substantial resources have been provided for startup funding. Ample newly renovated laboratory space is available.

Applicants should submit curriculum vitae; a statement of research interests and current grant support; a statement of teaching philosophy; and the names and contact information of three references to: **Dr. Robert J. Levis, Chairman, Department of Chemistry (016-00), Temple University, Beury Hall, 13th and Norris Streets, Philadelphia, PA 19122.** Review of applications will begin immediately and will continue until suitable candidates are identified.

Temple University is an Equal Opportunity/Affirmative Action Employer. The Department specifically invites and encourages applications from women and minorities.

NATIONAL UNIVERSITY of SINGAPORE
Department of Chemical and Biomolecular Engineering

The Department of Chemical and Biomolecular Engineering at National University of Singapore invites applications for **TENURE-TRACK FACULTY POSITIONS** at all levels. The Department is one of the largest internationally with excellent in-house infrastructure for experimental and computational research. A Ph.D. in chemical engineering or related areas and a strong research record with excellent publications are required. Please refer to **website: http://www.chbe.nus.edu.sg/** for more information on the areas of interest and for application details. Applicants should send full curriculum vitae (including key publications), a detailed research plan, a statement of teaching interest, and a list of names of at least three references to: **Professor Raj Rajagopalan, Head of Department (attention: Ms. Nancy Chia, e-mail: nancychia@nus.edu.sg).**

THE UNIVERSITY *of* NORTH CAROLINA

GREENSBORO

Professor and Head
Department of Biology

The Department of Biology at the University of North Carolina at Greensboro invites applications and nominations for the position of Department Head. The appointment will be at the rank of Professor with tenure and will be effective August 1, 2008. The Head is expected to provide effective administrative and intellectual leadership for the department, to support the faculty in their work as researchers and teachers, and to build connections for the department with the region and the state. The department has strong faculty research programs, which are supported by funding from agencies such as NIH, EPA, NSF and USDA. The department is currently planning a Ph.D. program, and the Head will work with the faculty to complete its planning and implementation. The department welcomes applications from individuals pursuing research in any area of biology, and particularly encourages those from applicants whose research would enhance the department's existing strengths. The applicant should have a strong record of research and teaching, including a history of obtaining competitively awarded external grants, and must also be committed to advancing the department's goal of building upon its nationally visible research profile. Previous administrative experience in a Ph.D. granting department will be an advantage.

The Department of Biology (**http://www.uncg.edu/bio**) is one of 21 departments in the College of Arts and Sciences and has approximately 760 undergraduate majors and 35 Master's students. The department has 23 tenured/tenure-track faculty positions and 15 full-time lecturers. It is anticipated that additional positions will be allocated to the department following the establishment of the planned Ph.D. program.

UNC Greensboro, one of 16 campuses in the University of North Carolina system, is classified by the Carnegie Foundation as a research university with high research activity. Enrollment is approximately 17,000 students, including 4,000 graduate students, in the College and six professional schools. Greensboro is a city of about 240,000 in the Piedmont Triad region of North Carolina, a location providing easy access to the Research Triangle and to recreational opportunities at the coast and the mountains. The local metropolitan area (which includes the cities of High Point and Winston-Salem) has a population of almost one million and offers an excellent quality of life. UNC Greensboro is especially proud of the diversity of its student body, and it seeks to attract an equally diverse applicant pool for this position, including women and members of minority groups.

Review of applications will begin on **November 1, 2007**, and will continue until the position is filled. Applicants should submit their vitae with a letter explaining their interest in the position, a description of their research program, a description of their approach to the responsibilities of a Department Head, and contact information for four references. Electronic submission of application materials is preferred and should be directed to **TANILE@UNCG.EDU**. Mailing address: **Dr. Terence A. Nile, Chair, Biology Headship Search Committee, Office of the Dean, 105 Foust Building, UNC Greensboro, Greensboro, NC 27402**. Inquiries and applications will be treated confidentially on request.

UNCG is an AA/EEO Employer with a strong commitment to increasing faculty diversity and will respond creatively to the needs of dual-career couples.

ASSISTANT PROFESSOR/ INFECTIOUS DISEASES
WASHINGTON UNIVERSITY SCHOOL OF MEDICINE

The Division of Infectious Diseases in the Department of Medicine at Washington University School of Medicine solicits applications for tenure-track appointments at the rank of Assistant Professor. We are seeking interactive individuals who will be able to establish a vigorous and outstanding independent basic research program. Our program has a strong emphasis on microbial pathogenesis in prokaryotic, viral and eukaryotic systems. Recruited faculty will be located contiguous to the Department of Molecular Microbiology and the Division of Pediatric Infectious Diseases; there is tremendous potential for collaborative interactions. Preference will be given to academic physicians who are board eligible/certified in infectious diseases. Very attractive start-up packages and protected time arrangements will be offered.

Applicants should send a detailed curriculum vitae, a few selected reprints, a brief description of current and planned research interests, and arrange to have three letters of reference sent to: **Daniel E. Goldberg, M.D., Ph.D., Co-Chief, Division of Infectious Diseases, Attn: Faculty Search Committee, Washington University School of Medicine, Campus Box 8230, 660 S. Euclid Ave., St. Louis MO 63110**.

WUSM is an Equal Opportunity/Affirmative Action Employer. Women and minorities are especially encouraged to apply.

Assistant Professor
Redox Biology Center and Department of Biochemistry
University of Nebraska-Lincoln (UNL)

The Redox Biology Center (RBC) at UNL, funded as a Center of Biomedical Research Excellence by the National Institutes of Health, invites applications for a **tenure-leading Assistant Professor** position in the Department of Biochemistry. Any area of redox biology will be considered, but we are particularly interested in applicants with expertise in bioinformatics/functional genomics, mass-spectrometry, and/or redox regulation/signaling. The RBC is a major focus group for research in redox biology, incorporating various investigators at UNL and the University of Nebraska Medical Center in nearby Omaha. Areas such as thiol-based redox signaling and gene regulation, redox control of neurodegenerative diseases, cancer and aging, biochemistry of redox-active trace elements, structural biology, proteomics/metabolomics, microbial pathogenesis and redox homeostasis are all current targets of investigation. The Center also operates mass-spectrometry and spectroscopy core research facilities. The successful applicant will be expected to establish an internationally recognized, federally funded research program. The associated teaching commitment will be one course per academic year at the undergraduate or graduate level. The position will be housed in the state-of-the-art George W. Beadle Center, and carries with it a 12-month, state-funded appointment and a generous start-up package. This hire is one of several new faculty positions that the RBC will fill in various areas of redox biology during the next four years. To learn more about the Center and the Department, please visit **http://www.unl.edu/RedoxBiologyCenter** and **http://biochem.unl.edu**.

To be considered for the position, please go to **https://employment.unl.edu** requisition **070703** and complete the Faculty/Academic/Administrative Application. Then under separate cover send a curriculum vitae, a succinct statement of research and teaching interests, and three letters of reference sent to: **Redox Biology Center Search Committee, Dr. Vadim Gladyshev, University of Nebraska, N118 Beadle Center, Lincoln, NE 68588-0662, USA** or email to **redox2@unl.edu**. Review of applications will begin on **October 19, 2007** and continue until the position is filled.

The University of Nebraska is committed to a pluralistic campus community through affirmative action and equal opportunity and is responsive to the needs of dual career couples. We assure reasonable accommodation under the Americans with Disabilities Act, contact Joyce Ore at (402) 472-3173 for assistance.

TENURE-TRACK FACULTY
The University of Miami at Coral Gables

As part of a significant expansion, the Department of Biology seeks a tenure-track candidate in developmental biology who uses nonmammalian model genetic organisms to investigate fundamental problems. Preferred candidate must be able to interface with one another and with the broader research community that has strong foci in neuroscience, evolution, and ecology. Application review will begin by October 1, 2007, and will continue until position is filled. The successful candidate will be expected to maintain innovative, externally funded research and to teach graduate and undergraduate students. Nine months of salary is guaranteed. Ph.D. and postdoctoral work is required. Send curriculum vitae, representative reprints, statements of research and teaching interests, and have three letters of reference sent to **e-mail: biosearch@bio.miami.edu.**

TENURE-TRACK POSITION
in Biomedical Sciences

The Department of Biomedical Sciences at the University of South Alabama (USA) seeks candidates for a tenure-track faculty position at the **ASSISTANT or ASSOCIATE PROFESSOR** level. The USA Biomedical Sciences Department offers a B.S. degree and is responsible for the undergraduate education of students interested in pursuing post baccalaureate study in medicine, health professions, or basic sciences. Candidates must have a Ph.D., or equivalent, in a biomedical science and two years of postdoctoral experience is preferred. The successful candidate will be expected to teach, develop an active research program, and mentor undergraduate research projects. Review of applications will begin on October 15, 2007, and will continue until the position is filled, with an estimated start date of June 1, 2008. Applications should include a cover letter of interest, curriculum vitae, and three letters of reference. The application material should be sent via regular mail or e-mail to: **Dr. Michael P. Spector, Professor, Department of Biomedical Sciences, UCOM 6000, University of South Alabama, Mobile, AL 36688-0002; telephone: 251-380-2710; fax: 251-380-2711;** or **e-mail: mspector@usouthal.edu. Website: http://www.southalabama.edu/alliedhealth/biomedical.** *The University of South Alabama is an Equal Opportunity/Equal Access Employer.*

FOUR OPENINGS in EXPERIMENTAL and THEORETICAL PHYSICS
University of California, Merced

The University of California at Merced invites applications for four tenured/tenure-track positions in physics, defined broadly as: (1) nanoscale physics (**ASSOCIATE or FULL PROFESSOR** level), (2) condensed matter physics (**ASSISTANT PROFESSOR** level), (3) atomic, molecular, and optical (AMO) physics (**ASSISTANT PROFESSOR** level), and (4) biophysics (open rank), with a special interest in biological or biologically inspired systems that pertain to the cellular, subcellular, or single molecule scales.

For all positions, both **Experimentalists** and **Theorists** are encouraged to apply. The University of California at Merced is the tenth campus of the University of California system and the first U.S. research university built in the 21st century. We seek distinguished scholars with a keen interest in founding a new university and establishing a creative, vigorous research program in a multidisciplinary environment. For more information or to apply, visit **website: http://www.ucmerced.edu/jobs/.** To ensure full consideration, complete applications should be received by November 30, 2007. *Affirmative Action/Equal Opportunity Employer.*

TENURE-TRACK POSITION in BIOCHEMISTRY
University of Wisconsin, Madison

The Department of Biochemistry at the University of Wisconsin, Madison **(website: http://www.biochem.wisc.edu)**, invites applications for a position in biochemistry at the **ASSISTANT PROFESSOR** level. Applications in all areas of biochemistry will be considered. The Department is particularly interested in candidates working with cutting edge technologies (nanotechnology, cellular imaging, proteomics/metabolomics/lipidomics) in animal, plant, or model organisms in research areas related to the chemistry of protein or nucleic acid function, regulation of metabolism, or neurobiology. The University and Department provide an excellent environment for the development of an outstanding research program. The successful candidate will be expected to develop a vigorous, extramurally funded, independent research program, and to participate in the undergraduate and graduate teaching programs of the Department. PDF applications should include curriculum vitae, a list of publications, and a brief summary of accomplishments and directions of future research and be sent to **e-mail: facultysearch@biochem.wisc.edu.** Three letters of reference should be forwarded to the same address with applicant's name in header. Applications should be completed by October 15, 2007.

JOB OPPORTUNITY in BIOCHEMISTRY FACULTY POSITION
Department of Biochemistry
Stanford University School of Medicine

Applications or nominations are invited for an **ASSISTANT PROFESSOR** position in the Department of Biochemistry. Applicants should have an established record of excellence in original research and teaching. The predominant criterion for appointment in the University tenure track is a major commitment to research and teaching. Candidates should submit curriculum vitae including a list of publications, a description of their research interests, and names, addresses, and telephone numbers of three references to **e-mail: biochemistry_recruitment@stanford.edu.** Applications should be received by October 31, 2007. Reference letters should be sent to the above e-mail address or to: **Search Committee Chairman, Department of Biochemistry, Stanford University School of Medicine, 279 Campus Drive, Room B400, Stanford, CA 94305-5307.**

Stanford University is an Equal Opportunity Employer and is committed to increasing the diversity of its faculty. It welcomes nominations of and applications from women and members of minority groups, as well as others who would bring additional dimensions to the University's research, teaching and clinical missions.

ASSISTANT PROFESSOR of CHEMISTRY

The Department of Chemistry of the University of Wisconsin, Madison, anticipates an opening for a faculty position to begin in August 2008. We seek outstanding candidates at the **ASSISTANT PROFESSOR** level (tenure track) in all areas of chemistry including chemical education. Candidates must have a Ph.D. in chemistry or a related field; postdoctoral experience is desirable. The position requires development of an internationally recognized program of scholarly research as well as excellent teaching at both the undergraduate and graduate levels. Please submit curriculum vitae and concise description of research plans online at **website: http://www.chem.wisc.edu.** Three letters of recommendation will also be required through the online service directed to: **Chair, Faculty Search Committee, Department of Chemistry, University of Wisconsin-Madison, 1101 University Avenue, Madison Wisconsin 53706-1322.** To guarantee full consideration, all materials must arrive before October 1, 2007.

The University of Wisconsin is an Equal Opportunity/Affirmative Action Employer; applications from qualified women and minority candidates are encouraged. Unless confidentiality is requested in writing, information regarding the identity of the applicant must be released.

TEMPLE UNIVERSITY SCHOOL of MEDICINE
Department of Biochemistry

Tenure-track faculty positions are available at the **ASSISTANT or ASSOCIATE PROFESSOR** level for candidates with strong research records in biochemistry, molecular biology, cell biology, biophysics, or related disciplines. The Department is expanding in the areas of cellular and molecular approaches to signal transduction, transcriptional control, and nuclear regulatory mechanisms. Related and other areas of interest will also be considered. Applicants should apply electronically to **e-mail: biochem@temple.edu.** Application information and links to the Department are available at **website: http://www.temple.edu/med/biochem/search.**

Temple University is an Affirmative Action/Equal Opportunity Employer and strongly encourages applications from women and minorities.

MOLECULAR GENETICS

Washington State University (WSU) Vancouver invites applications for full-time, tenure-track **ASSISTANT PROFESSOR** with research emphasis in molecular genetics in animal systems or other taxa that complement the strengths of existing faculty. Successful applicant will teach two courses per year, advise graduate and undergraduate students, and establish productive, externally funded research program. Excellence in research and instruction are the main criteria for selection. Minimum qualifications: Ph.D. in molecular biology, genetics, or related discipline by date of hire. Preferred candidates will demonstrate commitment to working with diverse student and community populations. WSU Vancouver is located across the Columbia River from Portland, Oregon, and offers significant opportunities for research and an excellent quality of life. Additional information is available at **website: http://www.vancouver.wsu.edu/programs/sci/.**

Applicants should submit curriculum vitae, copies of two publications, summary of research accomplishments, statement of teaching philosophy and interests, and three letters of reference to: **Molecular Genetics Search, Washington State University Vancouver, 14204 N.E. Salmon Creek Avenue, Vancouver, WA 98686-9600.** Review of completed applications will begin on October 15, 2007.

Washington State University is an Equal Opportunity/Affirmative Action Educator and Employer. Members of groups historically underrepresented in science are strongly encouraged to apply.

DIRECTOR, MOUNT SINAI MELANOMA CENTER
The Mount Sinai Medical Center
New York, New York

The Mount Sinai Medical Center is seeking an outstanding scientist to serve as the Director of the Mount Sinai Melanoma Center.

Mount Sinai is currently ranked among the top 20 medical schools in NIH funding and is committed to establishing one of the nation's premier cancer programs located in an academic full service medical center. Resources are being provided to recruit and retain the highest quality scientists and clinicians.

In an initiative co-sponsored by Mount Sinai's Departments of Oncological Sciences and Dermatology, the Director of the Melanoma Center will have the opportunity to build an outstanding comprehensive melanoma program with an emphasis on translational research leading to therapeutic breakthroughs. We invite applications from senior investigators with either a Ph.D. or M.D. and a strong research focus in melanoma. The successful candidate will receive generous startup funding for this program.

For consideration, please submit curriculum vitae, a statement of research interests, copies of three publications, and the names and contact information of three or more references to **e-mail: melanomasearch@mssm.edu.**

UNC-Chapel Hill SPH
NUTRITION RESEARCH INSTITUTE
at Kannapolis
exploring nutritional individuality

The **Nutrition Research Institute (NRI)** and the Department of Nutrition in the School of Public Health at the University of North Carolina at Chapel Hill are jointly recruiting for the following tenured or tenure track positions to be located in Kannapolis, NC (near Charlotte):

- A world-class research leader for the Nutrition and Obesity/Eating Disorders team of 4 to 5 faculty members.
- A world-class research leader for the Nutrition and Cancer team of 4 to 5 faculty members.
- Four faculty members to be part of the Nutrition and Brain Development research team.
- Three faculty members with methods expertise: metabolomics (1), nutrigenomics (1) and nutrient intake assessment (1) who will be part of all 3 research teams.

We offer: A world-class facility focusing on nutrigenomics and metabolomics as they apply to human nutrition • Hard money support for researchers • Excellent start-up packages • Brand new labs and office space • Capacity to do human and mouse research • Major investment in state-of-the-art instrumentation and equipment in metabolomics and nutrigenomics • Outstanding intellectual environment on campus with programs from 7 universities

For more information about the NRI or to apply, visit our website, **www.uncnri.org**.

We strongly encourage applications from women, minorities and individuals with disabilities. The University of North Carolina at Chapel Hill is an Equal Opportunity Employer.

University of California
San Francisco
UCSF

The Department of Urology at the University of California, San Francisco, is recruiting for two full-time faculty basic research scientists at the In-Residence or Adjunct series with an academic rank at the Assistant/Associate/Full level dependent on the applicant's level of experience. Applicant should have a Ph.D. or equivalent degree in one of the following areas: molecular biology, genetics, virology, microbiology, biochemistry or biology. Candidates should have solid research experience supported by a track record of publications and extramural funding, a genuine interest and expertise in teaching and conduct basic research within their subspecialty area. Send letter of interest and curriculum vitae to:

Peter R. Carroll, MD
Professor and Chair, UCSF Department of Urology
Attention: Penny Chee
400 Parnassus, A628
San Francisco, CA 94143-0738

UCSF seeks candidates whose expertise, teaching, research, or community service has prepared them to contribute to our commitment to diversity and excellence. UCSF is an Affirmative Action/Equal Opportunity Employer. The University undertakes affirmative action to assure equal employment opportunity for underutilized minorities and women, for persons with disabilities, and for covered veterans. All qualified applicants are encouraged to apply, including minorities and women.

RESEARCH FACULTY POSITIONS

The H. Lee Moffitt Cancer Center & Research Institute, an NCI-designated Comprehensive Cancer Center, and the University of South Florida College of Medicine's Department of Interdisciplinary Oncology are seeking candidates at the Assistant/Associate/Full Professor rank to participate in the Molecular Oncology Program. The successful candidates must possess a Ph.D. or M.D. degree and a demonstrated potential for extramural funding. Individuals with a research interest in proteomics are especially encouraged to apply, but any areas of gene regulation, signal transduction, cancer genetics, and functional genomics will be considered.

Applicants must have a proven track record of independent research and demonstrated sustained extramural funding. In addition, the Associate Professor rank requires at least five years experience with continuing and productive service as an Assistant Professor. The Professor rank requires documentation of national recognition, leadership ability and at least five years experience with continuing and productive service as an Associate Professor. The positions may be tenure earning and salary is negotiable.

Please reference position no. 12515. Interested candidates should send curriculum vitae and a brief statement of major academic interests in one single pdf document to The Molecular Oncology Search Committee at Rebecca.Koransky@moffitt.org. Application review begins September 7, 2007; the positions are open until filled.

H. LEE MOFFITT Cancer Center & Research Institute
The End Of Cancer Begins Here.
A National Cancer Institute Comprehensive Cancer Center
At the University of South Florida

USF HEALTH

USF Health is committed to increasing its diversity and will give individual consideration to qualified applicants for this position with experience in ethnically diverse settings, who possess varied language skills, or who have a record of research that supports/benefits diverse communities or teaching a diverse student population. The University of South Florida is an EO/EA/AA Employer. For disability accommodations, contact Kathy Jordan at (813) 745-1451 a minimum of five working days in advance. According to FL law, applications and meetings regarding them are open to the public.

www.moffitt.org

FACULTY POSITIONS

BIOANALYTICAL CHEMISTRY FACULTY POSITION. The Department of Chemistry at the University of Kansas is seeking exceptional candidates for a tenure-track, **ASSISTANT PROFESSOR** position in bioanalytical chemistry expected to begin August 18, 2008, or thereafter. This successful candidate will become a member of the Ralph N. Adams Institute for Bioanalytical Chemistry. The University supports a very collaborative and cross-disciplinary research environment, and shared instrumentation resources for bioanalytical research are outstanding. They include state-of-the-art microscopy equipment, an 800 MHz NMR, Fourier Transform and MALDI TOF/TOF mass spectrometer, and a microfabrication facility with a class 100 clean room, inductively coupled plasma reactive–ion etcher and plasma enhanced chemical vapor deposition.

The successful candidate will develop a vigorous research program in bioanalytical chemistry and teach at the undergraduate and graduate levels, so a Ph.D. in chemistry or a closely related field is expected by start date of appointment, and postdoctoral experience is desirable. Salary is competitive with those at other research universities.

Applicants should submit a letter of interest; curriculum vitae; a brief summary of two to three research proposals, two pages each; a two-page statement of teaching philosophy, expertise, and interests; and should arrange for the submission of three letters of recommendation to: **Jan Akers, Bioanalytical Search Committee Coordinator, 1251 Wescoe Hall Drive, Room 2010 Malott Hall, University of Kansas, Lawrence, KS 66045-7582. E-mail: jakers@ku.edu; telephone: 785-864-3471.** *Initial review of applications will begin October 1, 2007, and will continue until the position is filled. Equal Opportunity/Affirmative Action Employer.*

ASSISTANT PROFESSOR
Temple University
Department of Chemistry

The Department of Chemistry at Temple University invites applications and nominations for a tenure-track faculty position at the Assistant Professor level in the areas of biochemistry, organic or materials chemistry. Applicants are expected to demonstrate strong potential for establishing a vigorous research program funded by peer-reviewed research grants and for developing excellence in teaching. Salaries are highly competitive and substantial resources have been provided for startup funding. Ample newly renovated laboratory space is available.

Applicants should submit curriculum vitae; a statement of research interests and (if applicable) current grant support; a statement of teaching philosophy; and three letters of reference to: **Dr. Robert J. Levis, Chairman, Department of Chemistry (016-00), Temple University, Beury Hall, 13th and Norris Streets, Philadelphia, PA 19122.** Review of applications will begin immediately and will continue until suitable candidates are identified.

Temple University is an Equal Opportunity/Affirmative Action Employer. The Department specifically invites and encourages applications from women and minorities.

Montana State University Department of Microbiology seeks an infectious disease **MICROBIOLOGIST** for a tenure-track position at the **ASSISTANT, ASSOCIATE, or FULL PROFESSOR** level. Responsibilities include teaching at the undergraduate and graduate levels and developing or maintaining an extramurally funded research program. Candidates for this position should have current extramural funding. Competitive salary and startup funds are available. For more information and to apply please see our **website: http://www.montana.edu/cgibin/msuinfo/fpview/f/7404-2.** Screening of applications will begin October 15, 2007, and continue until the position is filled. *MSU, Bozeman, is an ADA/Affirmative Action/Equal Opportunity/Veterans' Preference Employer.*

FACULTY POSITIONS

IES

TWO ANTICIPATED POSITIONS in ECOSYSTEM SCIENCE
Institute of Ecosystem Studies

The Institute of Ecosystem Studies seeks two individuals at the level of **ASSISTANT or ASSOCIATE SCIENTIST.** The successful candidates will have a proven track record of research funding and publication in top scientific journals. We are particularly interested in research interests that relate to: (1) The impacts of global change on forest and associated ecosystems. Ecologists studying the future composition, biogeochemical function, and/or management of forested ecosystems in the face of climate change, exurban development, invasive species, or potential large-scale biofuel production are particularly encouraged to apply. (2) The ecology of infectious diseases. Ecologists studying zoonoses, wildlife diseases, and plant diseases caused by viral, bacterial, fungal, protozoan, or metazoan parasites are welcome to apply.

The Institute, a privately endowed research and education organization located on a 2,000-acre arboretum in the Hudson River Valley of New York, currently hosts a staff of 16 scientists, who investigate human impacts on forest, freshwater, and urban ecosystems. We seek individuals who can join this team and establish interdisciplinary collaborations that extend the Institute's work to consider human interactions with ecosystems, especially in light of global change. Visit us at **website: http://www.ecostudies.org.**

We will begin to review applications on 1 October 2007, with the anticipation of filling these positions in early 2008. Apply by sending curriculum vitae, statement of research interests and goals, and the names and addresses of three potential references to: **Human Resources, The Institute of Ecosystem Studies, Job Reference # 07029-SCI, P.O. Box AB, Millbrook, NY 12545; e-mail: jobs@ecostudies.org.** *The Institute of Ecosystem Studies is an Equal Opportunity/Affirmative Action Employer. Women and minorities are encouraged to apply.*

INORGANIC CHEMISTRY FACULTY SEARCH 2007-2008

ASSISTANT PROFESSORSHIP, INORGANIC CHEMISTRY. The Department of Chemistry at Washington University in St. Louis seeks to fill a position to begin in the fall 2008 in any area of inorganic chemistry including at the interfaces with biological and materials chemistry. The development and maintenance of an outstanding research program and the teaching of core chemistry courses at the undergraduate and graduate levels are required. Candidates must have a completed Ph.D. degree in hand at the time of appointment. Applications should consist of curriculum vitae and a concise research proposal or proposals. These documents are to be submitted in electronic form as PDF (portable document format) files to **e-mail: search@wuchem.wustl.edu** with the subject line "Inorganic Chemistry Faculty Search." Applicants should also arrange for three letters of reference to be sent to **e-mail: search@wuchem.wustl.edu,** with signed originals sent to:

Inorganic Chemistry Faculty Search Committee
Department of Chemistry
Campus Box 1134
Washington University
One Brookings Drive
St. Louis, MO 63130-4899
Fax: 314-935-4481

Completed applications for the position must be received by 15 October 2007, to ensure inclusion in the initial review. However, applications received later will be accepted and reviewed until a candidate has been hired or the search discontinued. *Washington University is an Equal-Opportunity, Affirmative-Action Employer. Individuals from underrepresented groups are especially encouraged to apply.*

FACULTY POSITIONS

RANDOLPH-MACON COLLEGE
Biology Department

The Department of Biology invites applications for two tenure-track positions at the rank of **ASSISTANT PROFESSOR** beginning August 2008. The department seeks an **EVOLUTIONARY BIOLOGIST** and an **ECOLOGIST.** The standard teaching load is two lecture/laboratory courses per semester, which is equivalent to a combination of lecture and lecture/laboratory courses that total 24 teaching credit hours. The successful candidates will teach annually in an innovative inquiry-based introductory biology course and will contribute to its ongoing development. They will also be expected to develop upper-level courses in their specialty. Ongoing scholarly activity involving undergraduates is expected. Applicants must have a Ph.D. and be able to demonstrate teaching effectiveness. Review of applications will begin on October 31, 2007, and continue until the positions are filled. Applicants should indicate which position they are applying for and submit: (1) curriculum vitae, (2) a statement of their teaching philosophy and research plans, and (3) three letters of reference. Applications and inquiries to: **Ms. Barb Wirth, Randolph-Macon College, P.O. Box 5005, Ashland, VA 23005.** *Applications are especially encouraged from minorities and women. Randolph-Macon College is an Equal Opportunity Employer.*

FACULTY OPENING
School of Chemical and Biomolecular Engineering

Located in Ithaca, New York, Cornell University is a bold, innovative, inclusive, and dynamic teaching and research University where staff, faculty, and students alike are challenged to make an enduring contribution to the betterment of humanity.

Cornell University invites applications for a tenure-track position in the School of Chemical and Biomolecular Engineering at any rank **(ASSISTANT, ASSOCIATE, or FULL PROFESSOR)** consistent with the candidate's experience and achievements. All research areas will be considered, with preference given to those in the broad area of biomolecular engineering.

Interested candidates can learn more about this position at **website: http://www.cheme.cornell.edu/news.**

Cornell is committed to being a supportive, family-oriented employer. Cornell University is an Affirmative Action/Equal Opportunity Employer and Educator. The School of Chemical and Biomolecular Engineering, and the College of Engineering, are committed to increasing the diversity of the faculty and we strongly encourage people from underrepresented minority backgrounds to apply.

FACULTY POSITION, HEARING and BALANCE. The Department of Otolaryngology, Head and Neck Surgery at Johns Hopkins University School of Medicine is recruiting a research faculty member studying auditory or vestibular neuroscience, with particular interest in molecular mechanisms and approaches. This position will be affiliated with the Center for Hearing and Balance **(website: http://webhost5.nts.jhu.edu/chb/),** an interdepartmental research cooperative spanning cellular to behavioral analyses of audition and balance. The position will be tenure-track and includes substantial laboratory space and startup funds. Additional funding may be available through an endowment dedicated to the study of Meniere's disease. Please send curriculum vitae, research plan, names of three references and up to three publications (PDF) no later than December 1, 2007, to **e-mail: otojob@jhmi.edu.** Recommendation letters should be sent to this same e-mail address. *Johns Hopkins University is committed to policies of Equal Opportunity and Affirmative Action which are essential to its mission of promoting research, service and academic excellence.*

Tulane University

FACULTY POSITION IN DEVELOPMENTAL BIOLOGY

The Department of Cell and Molecular Biology at Tulane University (**http://cell.tulane.edu/**) anticipates filling a tenure-track position beginning July 1, 2008, at the level of Assistant Professor. Targeted are individuals whose research interests focus in Developmental Biology, with an emphasis on mammalian organogenesis. The Department is undergoing a rebuilding process and has targeted Neuroscience and Developmental Biology as areas for rapid growth. Applicants must have a Ph.D., at least 2 years of postdoctoral experience, a strong publication record, and show strong potential for obtaining external funding. The successful applicant will be expected to establish a vigorous, independent research program and to participate in graduate and undergraduate teaching. Opportunities exist for research collaborations and participation in the Tulane Cancer Center, the Tulane Primate Center, the Center for Bioenvironmental Research, and the Tulane Neuroscience Program. Applicants should send curriculum vitae, a brief statement of research interests and three letters of recommendation by **December 1, 2007** to: **Dr. David Mullin, Chair, Department of Cell and Molecular Biology, Tulane University, 2000 Percival Stern Hall, New Orleans, LA 70118.**

Tulane University is an Equal Opportunity/ Affirmative Action Employer and encourages minority and female applicants to apply.

WESTFÄLISCHE WILHELMS-UNIVERSITÄT MÜNSTER

The Westfalian-University (Westfälische Wilhelms-Universität Münster) has recently founded a **European Institute of Molecular Imaging (EIMI)** initiated in a public-private-partnership between the university and Siemens Medical Solutions.

EIMI is a central academic institution of the University of Münster working in the field of developing, validating and applying molecular imaging techniques. EIMI is structured into two major areas of work, one being "Target Biology & Chemistry", the other "Technology & Imaging". The inter-faculty construct of EIMI, involving the faculties of medicine, chemistry and pharmacy, mathematics and computer sciences and physics, provides a broad spectrum of expertise from medicine, natural and computer sciences.

EIMI hereby offers the following position:

University Professor (W 3) for Target Biology & Chemistry

Candidates should have proven expertise in studies of basic molecular mechanisms of diseases, identification of molecular targets, design, breeding and surgery of wildtype and transgenic animal models, histology and tissue processing.

The position will initially have a limited tenure of 5 years. Prerequisite for the application are scientific achievements as a junior professor; alternatively, scientific achievements can result from a postdoctoral lecture qualification (habilitation), work as a research scientist at a school of higher education/university, non-university institute, industry, administration, or other fields of society within or outside Germany.

Applications are invited by physicians and natural scientists. Candidates are expected to participate in collaborative research of the existing Collaborative Research Centres (Sonderforschungsbereiche) of the university and in transfer of research results.

The future holder of the position will be expected to teach and examine relevant subjects.

Applications of women are specifically invited. In the case of equivalent qualification, competence, and specific achievements, women will be considered on preferential terms within the framework of the legal possibilities. Handicapped candidates with equivalent qualifications will be given preference.

Documents in support of an application, enclosing CV, scientific career, structured catalogue of publications, acquired third-party funds and reprints of the five most important publications should be submitted to the **European Institute of Molecular Imaging, Technologiehof Münster, Mendelstr. 11, 48149 Münster, Germany,** by **5th October 2007.**

FACULTY POSITION

Department of Molecular Biology Massachusetts General Hospital Department of Genetics Harvard Medical School

The Department of Molecular Biology at Massachusetts General Hospital and the Department of Genetics at Harvard Medical School invite applications for a joint appointment at the level of Assistant Professor. The laboratory will be located in the Massachusetts General Hospital Department of Molecular Biology (**http://molbio.mgh.harvard.edu**) and the faculty appointment will be in the Harvard Medical School Department of Genetics (**http://genetics.med.harvard.edu**).

Applicants should apply via electronic submission to the url listed below. Please submit a curriculum vitae, statement of research plans and up to three relevant publications, all in pdf format, by **November 15, 2007**. In addition, provide the names and email addresses of three references.

The URL for submission is:
http://molbio.mgh.harvard.edu/faculty_search/

Harvard University and the Massachusetts General Hospital are Equal Opportunity/ Affirmative Action Employers. We encourage applications from women and minorities.

UNIVERSITY of DAYTON

TWO TENURE-TRACK ASSISTANT PROFESSOR POSITIONS IN ECOLOGY
University of Dayton, Department of Biology, Dayton OH

The University of Dayton, Department of Biology invites applications for two Assistant Professor tenure-track faculty positions in Environmental Ecology, and Community/Conservation Ecology, to begin August 2008. These two positions are supportive of the Biology/Environmental Biology Degree programs and the Sustainability, Energy and the Environment (SEE) initiatives at the University of Dayton.

Position 1: Environmental Ecologist: The Department of Biology seeks to hire a tenure-track Environmental Ecologist at the Assistant Professor level. Areas of specialization may include the dynamics of environmental change, ecological succession, invasive species and ecological restoration. Preference will be given to ecologists working with plants or plant/animal interactions. The successful candidate will be expected to teach an undergraduate course in ecology, plant biology, ecological restoration or introductory biology and an undergraduate/graduate course appropriate to their specialty.

Position 2: Community/Conservation Ecologist: The Department of Biology seeks to hire a tenure-track Community/Conservation Ecologist at the Assistant Professor level. All levels and areas of ecological specialization will be considered. The successful candidate will be expected to teach an undergraduate course in ecology, conservation biology or introductory biology, and an undergraduate/graduate course appropriate to their specialty.

Requirements for both positions include a Ph.D., relevant post-doctoral experience and a commitment to excellence in research and teaching. The successful candidate will be expected to develop an extramurally funded research program which will involve Ph.D., M.S. and undergraduate students in his/her research program.

Please send a cover letter, curriculum vitae, selected reprints, at least three letters of recommendation, and statements of research interest and teaching philosophy by email to: **EcologySearch@notes.udayton.edu**, or send an electronic copy on CD to: **Dr. P. Kelly Williams, Chair of Search Committee, Department of Biology, University of Dayton, 300 College Park, Dayton, OH 45469-2320**. Copies of graduate transcripts will be required prior to interviewing. The Search Committee will begin reviewing applications by **November 15, 2007**, with on-campus interviews planned for early January, 2008. The search will continue until the positions are filled.

The University of Dayton is a private comprehensive research University located in the Columbus—Dayton-Cincinnati metroplex. Please visit our website: **http://biology.udayton.edu**.

The University of Dayton, a Comprehensive Catholic University founded by the Society of Mary in 1850, is an Affirmative Action/Equal Opportunity Employer. Women, minorities, individuals with disabilities, and veterans are strongly encouraged to apply. The University of Dayton is firmly committed to the principle of diversity.

FACULTY POSITIONS

ASSISTANT PROFESSOR of BIOLOGY

Penn State Erie, the Behrend College, invites applications for a tenure-track position in microbiology to begin August 2008. Candidates must have a strong commitment to undergraduate teaching and to research. Ph.D. required; postdoctoral and teaching experience preferred. Expectations: teach introductory microbiology with laboratory, ability to teach majors course in immunology is desirable, to alternate with upper-level course in field of expertise; establish an active research program involving undergraduates; seek external funding.

Penn State Erie is a four-year and graduate college of Penn State University with over 4,000 students. The College is committed to balance between teaching and research. The School of Science offers four-year majors in biology, chemistry, computer science, mathematics, physics, and general science. The faculty conducts research in ecology, molecular biology, developmental biology, genetics, and cell biology. Biology teaching and research laboratories are newly renovated and include a confocal microscope and a scanning electron microscopy facility. Pennsylvania Sea Grant is affiliated with Penn State Erie.

Erie, Pennsylvania, a metropolitan area of 280,000, is a major industrial, service, and tourism center on Lake Erie's Presque Isle Bay, located two hours from Cleveland, Pittsburgh, and Buffalo. The Erie region offers many cultural, sports, and academic resources, including five colleges and universities. Residents enjoy modest living costs and affordable housing.

Send curriculum vitae, copies of graduate and undergraduate transcripts, teaching and research statements, including a brief explanation of suitability of research at an undergraduate college, and names and e-mail addresses of three references to: **Dr. Roger Knacke, Penn State Erie, School of Science, Department BIOL-A , 4205 College Drive, Erie, PA, 16563-0203.** Application screening will begin October 26, 2007, and continue until the position is filled.

Penn State is committed to Affirmative Action, Equal Opportunity and the diversity of its workforce.

ORGANIC CHEMISTRY FACULTY POSITION
University of California, Los Angeles (UCLA)

As part of a hiring campaign to make multiple tenure-track faculty appointments in core and interdisciplinary areas of Chemistry, the Organic Division at UCLA invites applications for a tenure-track position at the **ASSISTANT PROFESSOR** level in all areas of organic chemistry, including but not limited to, organic materials, organic synthesis, physical organic chemistry, and chemical biology. Applicants are expected to have earned a Ph.D. degree in organic chemistry, and to be strongly committed to both teaching and research. Successful applicants will show evidence of exceptional originality and promise, and aspire to establish a world-class research program in a stimulating environment that fosters collaboration and values diversity. Applicants should mail curriculum vitae (including research accomplishments, teaching experience, and publications), a detailed research and teaching plan, and supporting letters from at least three references. Completed applications should be received by October 31, 2007, and directed to:

Chair of the Organic Search Committee
Department of Chemistry and Biochemistry
University of California, Los Angeles
P.O. Box 951569
Los Angeles, CA 90095-1569

The University of California, Los Angeles, and the Department of Chemistry and Biochemistry are interested in candidates who are committed to the highest standards of scholarship and professional activities, and to the development of a campus climate that supports equality and diversity. Women and minorities are encouraged to apply. The University of California is an Affirmative Action/Equal Opportunity Employer.

POSITIONS OPEN

FRED HUTCHINSON CANCER RESEARCH CENTER

A LIFE OF SCIENCE

M.D. or M.D./Ph.D. PHYSICIAN/SCIENTIST or Ph.D. TRANSLATIONAL SCIENTIST
Position Available
Fred Hutchinson Cancer Research Center
Seattle, Washington

The Fred Hutchinson Cancer Research Center (FHCRC) is recruiting a faculty member at the **ASSISTANT, ASSOCIATE, or FULL MEMBER** level with active laboratory research related to breast cancer. Physician/Scientists with strong laboratory research and clinical expertise in a breast cancer-related discipline or Ph.D. candidates with active translational research interests in breast cancer are strongly encouraged to apply. The successful candidate will join the large Breast Cancer Research group within the FHCRC/University of Washington Cancer Consortium; a dynamic cross-disciplinary research team dedicated to improving prevention, detection, diagnosis, prognosis, and treatment of breast cancer. The primary appointment will be in the Clinical Research Division of the FHCRC. If desired, a joint appointment may be made to other divisions at the Center and to the full-time faculty in an appropriate department at the University of Washington.

Interested individuals should forward their curriculum vitae, including a research plan and the names of five references, to: **Suzanne Lentz, Fred Hutchinson Cancer Research Center, 1100 Fairview Avenue N., Mail-Stop: C1-015, P.O. Box 19024, Seattle, WA 98109.** The closing date for applications is November 1, 2007.

The Fred Hutchinson Cancer Research Center is an Affirmative Action, Equal Opportunity Employer. We are dedicated to building a culturally diverse faculty and strongly encourage applications from women, minorities, individuals with disabilities, and covered veterans.

FACULTY POSITIONS

BIO-ORGANIC CHEMIST. The Williams College Chemistry Department invites application for a tenure-track position at the **ASSISTANT PROFESSOR** level for fall 2008. Senior appointment possible in exceptional circumstances. Initial teaching assignment, depending upon the successful candidate's subspecialty, will include two courses from: sophomore-level organic chemistry, enzyme kinetics and reaction mechanisms, biochemistry, and a course for nonscience majors. A semester teaching load normally includes complete responsibility for one course and two laboratory sections, and supervision of student research projects. Candidates should have the Ph.D. or completed dissertation by September 2008 (postdoctoral experience is preferred). The successful candidate must have a strong commitment both to teaching at the undergraduate level and to developing a productive research program. Williams College is a highly selective, coeducational liberal arts institution of approximately 230 faculty and 2,000 undergraduates, located in northwestern Massachusetts. The Chemistry Department is composed of 12 faculty members and graduates about 25 to 30 majors each year; the Department has excellent facilities for teaching and research. The College is actively working to increase the diversity of its science majors and seeks an individual who can help us meet these goals. Mail resume, undergraduate and graduate transcripts, descriptions of teaching philosophy and research projects for undergraduates, and three letters of recommendation to: **Prof. Enrique Peacock-López, Chair, Department of Chemistry, Williams College, Williamstown, MA 01267,** by November 12, 2007. Electronic applications will not be accepted. For additional information about the Chemistry Department, please visit our **website: http://www.williams.edu/Chemistry.**

Williams College is an Equal Opportunity/Affirmative Action Employer.

POSITIONS OPEN

The Division of Public Health Sciences of the Fred Hutchinson Cancer Research Center invites applications from laboratory-based scientists with an interest in molecular diagnostics, including but not limited to aspects of predictive medicine, early detection, diagnosis, treatment response, and risk assessment.

Further information is available at **website: http://www.fhcrc.org/about/jobs/** and selecting job posting identification # KW-21205.

FACULTY POSITIONS

INORGANIC CHEMIST. The Williams College Chemistry Department invites applications for a tenure-track position at the **ASSISTANT PROFESSOR** level for fall 2008 in the general area of inorganic chemistry. (Senior appointment possible in exceptional circumstances.) Initial teaching assignment, depending upon the successful candidate's subspecialty, will include two courses from: introductory chemistry, sophomore inorganic and physical chemistry, advanced inorganic/organometallic chemistry, and instrumental methods of analysis. A semester's teaching load normally includes complete responsibility for one course and two laboratory sections, and supervision of student research projects. Candidates should have the Ph.D. or completed dissertation by September 2008 (postdoctoral experience is preferred). The successful candidate must have a strong commitment both to teaching at the undergraduate level and to developing a productive research program. Williams College is a highly selective, coeducational liberal arts institution of approximately 230 faculty and 2,000 undergraduates, located in northwestern Massachusetts. The Chemistry Department is composed of 12 faculty members and graduates about 25 to 30 majors each year; the Department has excellent facilities for teaching and research. The College is actively working to increase the diversity of its science majors and seeks an individual who can help us meet these goals. Mail resume, undergraduate and graduate transcripts, descriptions of teaching philosophy and research projects for undergraduates, and three letters of recommendation to: **Prof. Enrique Peacock-López, Chair, Department of Chemistry, Williams College, Williamstown, MA 01267,** by November 12, 2007. Electronic applications will not be accepted. For additional information about the Chemistry Department, please visit our **website: http://www.williams.edu/Chemistry.**

Williams College is an Equal Opportunity/Affirmative Action Employer.

ASSISTANT PROFESSOR
Department of Biological Sciences
Murray State University

Full-time, tenure-track position to begin August 2008. Qualifications: Ph.D. with research interests at the cellular level required. Specific research areas are open: cellular bioinformatics, cell signaling, or cell differentiation are preferred. Must demonstrate a strong commitment to establishing a research program involving undergraduate and graduate students. Postdoctoral experience preferred; recent Ph.D. graduates with a strong publication record and the potential to attract extramural funding will be considered.

Responsibilities: Teach undergraduate and graduate level courses commensurate with departmental needs and the individual candidate's expertise. Application deadline: Postmarked by October 15, 2007. To apply: Submit letter of application, curriculum vitae, statement of teaching interest and philosophy, description of research, relevant reprints, copies of transcripts, and three letters of recommendation to: **Sterling N. Wright, Ph.D., Chair-Cellular Biology Search, Department of Biological Sciences, 2112 Biology Building, Murray State University, Murray, KY 42071.** *Women and minorities are encouraged to apply. Murray State University is an Equal Education and Employment Opportunity, Minorities/Females/Persons with Disabilities, Affirmative Action Employer.*

Faculty Position in Princeton Neuroscience Institute

Princeton University is seeking to make the first of several anticipated new faculty appointments in systems neuroscience, as part of the new interdisciplinary Princeton Neuroscience Institute, with a focus on quantitative approaches to understanding neural coding and dynamics.

The position is at the junior level (assistant professor) for a neuroscientist, with a preference for someone using advanced genetic and physiological techniques to dissect neural circuits. The appointment will be joint between the Institute and the Molecular Biology department.

Applicants should be prepared to participate in teaching neuroscience at both the undergraduate and graduate levels. Please send curriculum vitae, a two-page research description, and three letters of recommendation by email to **neurosearch@princeton.edu**. All materials must be submitted as PDF files. The application deadline is **October 15, 2007**.

For further information about applying to Princeton and how to self-identify, please link to **http://www.princeton.edu/dof/applicantsinfo.htm**.

Princeton University is an Equal Opportunity Employer and complies with applicable EEO and affirmative action regulations.

The UC Davis Genome Center integrates experimental and computational approaches to address key problems at the forefront of genomics. The Center is housed in a new research building with state-of-the-art computational and laboratory facilities and currently comprises 15 experimental and computation faculty. These faculty are developing an internationally recognized program in genomics and computational biology at Davis, building on and enhancing the unique strengths and unmatched breadth of the life sciences on the UC Davis campus.

The Genome Center invites applications for a tenure-track faculty position in computational and experimental approaches to network and synthetic biology. Candidates may be at any academic level. At the senior level, we invite applications from prominent scientists with distinguished records of research, teaching, and leadership in analysis and manipulation of biological networks. At the junior level, we invite applications from candidates whose accomplishments in innovative research and commitments to teaching demonstrate their potential to develop into the future leaders of these fields.

Candidates should be strongly motivated by the biological importance of their research and should value the opportunity to work in close collaboration with other groups. The Genome Center welcomes applications from strong candidates in all areas of networks and synthetic biology involving medical, animal, plant or microbial systems. Investigators employing large-scale approaches that complement existing strengths at UC Davis are particularly encouraged to apply.

This position requires a Ph.D. or equivalent. Candidates should be strongly motivated by the biological importance of their research and should value the opportunity to work in close collaboration with other groups. This appointment will be at the Assistant, Associate or Full Professor level in an appropriate academic department in any of six schools, or colleges. The position will remain open until filled. For fullest consideration, applicants should submit a letter of application, a curriculum vitae, statements of research and teaching interests, and the names of at least five references to the Genome Center Web site **www.genomecenter.ucdavis.edu** by **November 1, 2007**.

The University of California is an Affirmative Action/Equal Opportunity Employer.

Chemical Biology/ Medical Research

The OHSU Department of Physiology and Pharmacology invites applications for **tenure-track** faculty positions from individuals with a solid chemistry background interested in applying the tools and techniques of chemistry to biological and biomedical research. We are especially interested in candidates having a strong background in organic synthesis and research interests targeting important areas in biology and medicine.

Preference will be given to candidates for the position of **Assistant Professor,** but exceptional candidates for the position of **Associate** and **Full Professor** will also be considered. We seek individuals who will develop an independent research program, contribute to the teaching of medical and graduate students and interact with investigators studying drug metabolism, signal transduction, ion channel biology, G-protein coupled receptors and cardiovascular and reproductive biology.

OHSU offers a highly interactive research environment and superb opportunities for career development in a spectacular Pacific Northwest setting. A complete application consists of a curriculum vitae, a brief summary of research accomplishments, an outline of future research plans, and three letters of recommendation.

Applications and letters of recommendation may be directed to:
Thomas S. Scanlan, Ph.D.
Professor of Physiology and Pharmacology and
Director, Program in Chemical Biology,
Faculty Search (CB)

Dept. of Physiology and Pharmacology
Mail code L334
Oregon Health & Science University
3181 S.W. Sam Jackson Park Road
Portland OR, 97239-3098

OREGON HEALTH & SCIENCE UNIVERSITY

OHSU is an equal opportunity, affirmative action institution.

Tenure Track Faculty Position in Virology Indiana University Bloomington

The Microbiology Program in the Indiana University Department of Biology (**http://www.bio.indiana.edu**) invites applications for a tenure-track faculty position in Virology, including viral molecular, cellular, and systems biology, virus or bacteriophage structure and assembly, host-pathogen interactions, and virus evolution. This position is part of a significant, continuing expansion in the life sciences at IU Bloomington and represents an exceptional opportunity to join a strong Microbiology Program and new interdisciplinary initiatives linked to Human Biology, Biochemistry, Plant Biology, Biotechnology, Systems Biology, and the Medical Sciences. The successful candidate will be provided with a competitive startup package and salary and will have access to outstanding research resources and cutting-edge core facilities, including biocontainment facilities. The successful candidate will be expected to develop a vigorous externally funded research program and to participate in undergraduate and graduate teaching. Appointment is expected to be at the Assistant Professor level, but outstanding senior-level candidates will also be considered.

Applicants should mail a **curriculum vitae**, a statement of research (past, present, and planned) and teaching interests, and representative publications and preprints to: **Virology Search Committee c/o Jeremy Bennett, Department of Biology, Indiana University Bloomington, Jordan Hall, Room 142, Bloomington, IN 47405**. Please arrange to have at least four letters of recommendation sent by E-mail to: **jebennet@indiana.edu**. Questions should be addressed to Malcolm Winkler (**mwinkler@bio.indiana.edu**). Review of completed applications will begin immediately and continue until the position is filled.

Indiana University is an Affirmative Action/Equal Opportunity Employer. Women and minority candidates are encouraged to apply.

FACULTY POSITIONS OPEN
INSTITUTE OF MOLECULAR BIOLOGY
ACADEMIA SINICA, TAIWAN, ROC

Two tenure-track faculty positions are open for highly qualified individuals to establish independent research programs in **all areas of molecular and cellular biology** that would complement or strengthen the current topics in the Institute, including biochemistry, structural biology, developmental biology, immunology, and plant biology. However, individuals with innovative approaches that would lead to a new research program are also highly encouraged. Applicants should have a Ph.D. degree or its equivalents, and postdoctoral research experience is preferred. Successful candidates will be appointed at the levels of **Assistant, Associate**, or **Full Research Fellows** (the equivalents of Assistant, Associate and Full Professors in universities), with a generous multi-year start-up fund, followed by annual intramural support.

The Institute of Molecular Biology (**http://www.imb.sinica.edu.tw/en**) is an active and stimulating research environment: well supported by both intramural and extramural fundings, providing highly supportive cores such as imaging, genomics, bioinformatics and mouse facilities, and maintaining close international connections and strong interactions with local universities. Currently three Ph.D. programs, with one recruiting international students, are formally affiliated with the Institute. English is the official language for regular seminars and most of the lectures in the Institute, and proficiency in the Chinese language is not a prerequisite for application.

Applicants should send their Curriculum Vitae, a description of past research accomplishments and future research interests, and three letters of reference to:

Dr. Meng-Chao Yao, Director
c/o Ms. Vivi Chiang
Institute of Molecular Biology,
Taipei, Taiwan 11529, ROC

The selection process will start on December 31, 2007 until the positions are filled. Further information can be obtained from **Ms. Vivi Chiang at vivi@imb.sinica.edu.tw**

AUBURN UNIVERSITY
COLLEGE OF SCIENCES AND MATHEMATICS

Chair, Department of Biological Sciences

The Department of Biological Sciences at Auburn University invites applications and nominations for the position of Chair. Biological Sciences is an integrative department within the College of Sciences and Mathematics with expertise in a diverse array of biological disciplines offering M.S. and Ph.D. degrees to ~100 graduate students and B.S. degrees to ~550 undergraduate majors. More information about the department is available at **http://www.auburn.edu/biology**. A nationally recognized program of excellence in biological sciences has been identified as a University priority, and several new departmental faculty lines are anticipated in the next two years.

Applicants must have a Ph.D. in Biological Sciences or closely related life sciences discipline, as well as a record of academic excellence consistent with appointment as Full Professor. Dynamic leadership and strong interpersonal skills also are required. The Chair functions as an administrative scholar, providing visionary leadership to carry the Department of Biological Sciences forward in the areas of research, teaching, and outreach. The candidate selected for this position must be able to meet eligibility requirements to work in the U.S. at the time the appointment is scheduled to begin and continue working legally for the proposed term of employment and be able to communicate effectively in English.

Applicants should submit a detailed curriculum vitae, transcripts, representative reprints, a statement of administrative philosophy, personal teaching and research goals, and the names and contact information of at least three references. Applications should be sent to: **Dr. Charles Savrda, Biological Sciences Search Committee Chair, Dept. of Biological Sciences, 101 Life Sciences Building, Auburn University, AL 36849-5407**, or electronically as PDFs to **bioscichairsearch@auburn.edu**. Review of applications will begin **November 1, 2007**.

AUBURN UNIVERSITY IS AN AFFIRMATIVE ACTION/EQUAL OPPORTUNITY EMPLOYER. Women and minorities are encouraged to apply.

DANA-FARBER CANCER INSTITUTE

Dedicated to Discovery...Committed to Care.

ASSISTANT PROFESSOR
Tenure Track

Neurobiology/Oncology

The Dana-Farber Cancer Institute has launched a new program on low-grade astrocytomas and related brain tumors in children. Dana-Farber now seeks well-qualified applicants for a tenure-track position at the Assistant or Associate Professor level, with appointment in the Department of Neurobiology at Harvard Medical School or Pediatric Oncology at Children's Hospital, as appropriate. Candidates are expected to direct innovative and independent research on fundamental problems that underlie pediatric brain tumors and to participate in the teaching missions of the Institute and of Harvard Medical School. Developmental neurobiology and neuropathology are two areas of focus for the search. The position offers an attractive start-up support package in a stimulating scientific environment. Applicants must hold a Ph.D., M.D./Ph.D. or M.D. degree, have completed post doctoral training, and have a strong record of research accomplishments. Applications from women and minority candidates are encouraged.

Applicants should submit a curriculum vitae including a full list of publications, a brief statement of previous contributions and future research plans as well as the names and contact information of four references to:

Faculty Search Committee
c/o Deborah Goff
Dana-Farber Cancer Institute
Room SM1068, 44 Binney Street, Boston, MA 02115
E-mail: deborah_goff@dfci.harvard.edu

HARVARD MEDICAL SCHOOL

Applications must be received by November 1, 2007

The Dana-Farber Cancer Institute is an Equal Opportunity Employer.

SHARE THE VISION. FIND THE CURE

UNIVERSITY OF CALIFORNIA, SAN DIEGO
SCHOOL OF MEDICINE
FACULTY POSITIONS IN REPRODUCTIVE BIOLOGY

The University of California, San Diego has launched a major expansion of its renowned reproductive research programs, with plans to recruit three or more additional basic scientists at the Assistant, Associate or Full Professor level. Applications are particularly encouraged from scientists with programs in early mammalian developmental biology, neuroendocrinology, placentation, pregnancy, ovarian biology or cancer, connective tissue engineering, germ cell and human embryonic stem cell research. Applicants must hold a Ph.D. degree and will be expected to teach students, conduct an extramurally funded research program, and participate in administrative functions of the department and the University. Ample recruitment packages and excellent research space are available. The successful candidate will benefit from our highly stimulating and collaborative environment and top-ranked graduate programs.

Applicants are encouraged to submit a letter of interest, curriculum vitae, separate statements of research and teaching interests, and a list of five references to: **Dr. Pamela Mellon (pmellon@ucsd.edu), UCSD, Department of Reproductive Medicine, 9500 Gilman Drive, La Jolla, CA 92093-0674**. Applicants are welcome to include in their cover letters a personal statement summarizing their contributions to diversity. Review of applications will begin **October 15, 2007**, and will continue until the positions are filled.

The University of California, San Diego is a campus of the University of California, the preeminent higher education system in the world. It is located in the heartland of La Jolla surrounded by the Salk/Scripps/Burnham Institutes and 500-plus biotechnology companies. The series and level of the appointments, which may include the tenure-track/tenured ranks, will be commensurate with qualifications and experience. Salary will be based on published UC pay scales.

The University of California, San Diego, is an Affirmative Action/Equal Opportunity Employer with a strong institutional commitment to the achievement of diversity among its faculty and staff.

ASSISTANT/ASSOCIATE PROFESSORS

Departments of Molecular Genetics and Pediatrics

The Departments of Molecular Genetics and Pediatrics (**http://www.aecom.yu.edu/home/**) are jointly seeking candidates for two faculty positions at the Assistant or Associate Professor level.

We are particularly interested in the areas of developmental genetics and translational research involving human subjects and vertebrate model organisms. However, candidates working in any area of developmental biology or human genetics are encouraged to apply.

Applicants should submit curriculum vitae, the names of three references and a short description of their research plans to: **Faculty Search, Vivian Gradus, Dept. of Molecular Genetics, Albert Einstein College of Medicine, Jack & Pearl Resnick Campus, 1300 Morris Park Ave, Bronx, NY 10461; Email: gradus@aecom.yu.edu.** EOE

ALBERT EINSTEIN COLLEGE OF MEDICINE OF YESHIVA UNIVERSITY

Faculty Positions

Vollum Institute and Jungers Center
Oregon Health & Science University, Portland OR

The Vollum Institute (**http://www.ohsu.edu/vollum**) and the Jungers Center in association with the Department of Neurology announce faculty openings for outstanding scientists. For the **Vollum search**, we are particularly interested in individuals with a research focus in the general areas of *molecular and cellular neuroscience, molecular genetics, development and/or mechanisms of signal transduction*. For the **Jungers search**, we are interested in individuals whose work addresses *neurological diseases, especially the fundamental causes and treatments of neural injury and neurodegeneration as well as mechanisms of neural repair and regeneration*. Laboratory space is available in the Vollum Institute and the adjoining new Biomedical Research Building (**http://www.ohsu.edu/ohsuedu/about/transformation/brb**). It is expected that Jungers faculty will hold appointments in the Vollum Institute and the Department of Neurology. Vollum and Jungers appointments are fulltime research positions with minimal teaching or clinical requirements. Ample opportunities are available for collaboration with clinical units within the School of Medicine as well as research units at OHSU (**www.ohsu.edu**).

Applications will be considered at all levels. We offer attractive start-up packages and the opportunity to work in an outstanding scientific environment. Applicants should have a strong record of research and an interest in training graduate students. OHSU is an equal opportunity/affirmative action employer committed to maintaining diversity in its faculty. Candidates with a Ph.D. and/or M.D. and at least several years of postdoctoral experience should apply by sending one paper copy, and an electronic copy, of their curriculum vitae, a description of research plans and goals, and three references by **November 1, 2007** to:

Gary L. Westbrook, M.D.
Senior Scientist and Co-Director
Vollum Institute and Jungers Center Search
Vollum Institute, L474
Oregon Health & Science University
3181 SW Sam Jackson Park Road
Portland, OR 97239-3098
volljob@ohsu.edu

OREGON HEALTH & SCIENCE UNIVERSITY

FACULTY POSITION IN DEVELOPMENTAL BIOLOGY

The University of Georgia invites applicants for a tenure track Assistant Professor position in **developmental biology**. Applicants from any area of developmental biology are welcome; those working in mouse and/or zebrafish are especially encouraged to apply. The successful candidate's laboratory will be housed in the new Coverdell Center in an interactive, interdisciplinary faculty group with diverse research interests that provide a supportive environment for developmental biology research. The Coverdell Center has state of the art animal facilities for mouse and zebrafish research. The position includes a competitive salary, excellent laboratory space, and a generous start-up package. The successful candidate will be expected to develop a strong extramurally funded research program, and contribute to teaching in the department of appointment. This position is part of a planned multi-position expansion of the Interdepartmental Developmental Biology Group at UGA, which currently includes faculty from seven departments. Departmental affiliation will depend on the candidate's research focus. For more on the Developmental Biology Group at UGA, see **http://devbio.uga.edu**.

Applications received by **December 1, 2007** are assured of full consideration. Please email a CV, research and teaching statements, the names of three references, and up to three publications (all in PDF format please) to **pabond@uga.edu**. Emailed letters are acceptable if followed by an original. Letters of recommendation should be mailed to:

Dr. Nancy R. Manley
Associate Professor and Chair
Developmental Biology Group
S270A Coverdell Center for Biomedical and Health Sciences
University of Georgia, Athens, Georgia 30602

The Franklin College of Arts and Sciences is highly committed to increasing the diversity of its faculty and strongly encourages applications from members of under-represented groups. The University of Georgia is an Affirmative Action/Equal Opportunity Employer.

CANCER BIOLOGIST

The Ben May Department for Cancer Research
The University of Chicago

The University of Chicago is seeking applicants for a tenure-track position at the Assistant, Associate or Professor level. The Ben May Department for Cancer Research (**http://huggins.bsd.uchicago.edu**) is a basic research unit that for over 50 years has been committed to the study of cell signaling mechanisms. Our Department is located in the new Gordon Center for Integrative Sciences that comprises faculty from Chemistry, Physics and the Biological Sciences. The current faculty is committed to an interdisciplinary approach using established and newly emerging biochemical, genetic, imaging, molecular and structural biological tools to attack basic problems in signal transduction. We are seeking outstanding individuals interested in diverse aspects of tumor progression and metastasis, including, but not limited to, mouse models or other model organisms, drug discovery, proteomics, bioinformatics, genomics and computational biology.

The Ben May Department is closely affiliated with graduate degree-granting programs in the Biological and Physical Sciences, and Department faculty have access to outstanding PhD and MD/PhD students. Candidates should have sufficient research experience to demonstrate both significant accomplishments and outstanding potential. The successful recruit will be expected to teach undergraduate and graduate students. Curriculum vitae, bibliography, a brief statement of research interest and three letters of recommendation should be sent to: **Geoffrey Greene, Vice Chair, Ben May Department for Cancer Research, Gordon Center for Integrative Sciences, 929 East 57th Street, Room W330, Chicago, IL 60637.**

THE UNIVERSITY OF CHICAGO

The University of Chicago is an Affirmative Action/ Equal Opportunity Employer.

WAKE FOREST UNIVERSITY®
SCHOOL of MEDICINE
THE BOWMAN GRAY CAMPUS

FACULTY POSITIONS IN VIROLOGY

The Department of Microbiology and Immunology of Wake Forest University School of Medicine is seeking candidates to fill two tenure-track **ASSISTANT** and **ASSOCIATE** or **FULL PROFESSOR** positions in virology beginning July 2008. We are particularly interested in individuals with research programs in virus-host cell interactions and/or viral pathogenesis. Successful candidates will be expected to establish and maintain independent research programs and to participate in teaching of graduate and medical students.

The Department has a highly collaborative, research-intensive faculty and an outstanding graduate program that is supported, in part, by an NIH training grant in Immunology and Pathogenesis. In addition to strong individual NIH-sponsored research programs, Departmental faculty were awarded a 5 year, $9.2 million NIH program project grant entitled "Respiratory Immunity Against Agents of Bio-terrorism." This grant is one element in a Department-wide focus on viral and bacterial pathogenesis and immunity. Information on the Department, as well as links to the North Carolina community may be viewed at **www.wfubmc.edu/microbio**.

Review of applications will begin in **September, 2007** and will continue until the positions are filled. Applicants should submit a curriculum vitae, a brief description of current and future research interests, and arrange to have three letters of recommendation sent to:

Dr. Griffith D. Parks
Department of Microbiology and Immunology
Wake Forest University Health Sciences
Medical Center Blvd. Winston-Salem, NC 27157-1064
(email: gparks@wfubmc.edu)

Wake Forest University Health Sciences is an Equal Opportunity/ Affirmative Action Employer.

UTMB
The University of Texas Medical Branch

Tenure Track Faculty Position

The newly established Sealy Center for Molecular Medicine, in partnership with the Department of Biochemistry and Molecular Biology, seeks an outstanding individual for a tenure track faculty position at the Assistant/Associate Professor level. Current active programs include DNA damage repair, mechanism, characterization of DNA repair interactions, genetic susceptibility to environmental factors, regulation and post-translational modification of DNA repair genes, as well as other aspects of molecular signaling responses to oxidative stress. A PhD degree and at least five years of research experience with strong evidence of productivity and grant support are required. Successful candidates are expected to excel in mentoring graduate and postgraduate trainees. The ideal candidate should develop or continue a strong extramurally supported research program, and contribute to a collaborative research environment with additional opportunities for interactions with investigators in centers of scientific excellence in aging, cancer, infectious diseases, structural biology and environmental health.

To apply, please send a C.V. and names of four references to:

Werner Braun, PhD
Vice-Chair, Biochemistry and Molecular Biology
The University of Texas Medical Branch
301 University Blvd.,
Galveston, TX, 77555-0645
Email: webraun@utmb.edu

UTMB is an Equal Opportunity/Affirmative Action Institution that proudly values diversity. Candidates of all backgrounds are encouraged to apply.

Tenure-Track Faculty Position in Protein Structure and Function Research

As part of our continuing efforts to build strength and excellence in the area of structural and functional analysis of macromolecules, the Department of Biochemistry and Molecular Biology at the University of Texas M. D. Anderson Cancer Center is looking for an interactive scientist able to develop a world-class research program employing cutting-edge biophysical and biochemical approaches to understand cellular processes at the level of single molecules and their germane complexes. Applicants should have expertise in enzymology, calorimetry, chemical biology, spectroscopy or other physical approaches. Applicants, who complement and expand our strengths in gene regulation, developmental biology, signal transduction, structural biology and epigenetics, will be preferred. This tenure-track position is at the rank of Assistant Professor. However, outstanding scientists at higher rank will be considered. The Department will offer a generous start-up package and membership in the Center for Structure, Chemistry and Function of Macromolecules will provide access to cutting-edge technologies. Please send your CV, contact information of three references and a three-page summary of your research program to:

Dr. Richard G. Brennan, Chair
Structure and Function Search Committee
at sfsearch@mdanderson.org
The application deadline is December 3, 2007.

THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER
Making Cancer History®

M. D. Anderson Cancer Center is an equal opportunity employer and does not discriminate on the basis of race, color, national origin, gender, sexual orientation, age, religion, disability or veteran status except where such distinction is required by law. All positions at The University of Texas M. D. Anderson Cancer Center are security sensitive and subject to examination of criminal history record information. Smoke-free and drug-free environment.

Assistant or Associate Professor
Department of Cell & Developmental Biology

Applications are invited for a tenure-track position at the Assistant or Associate Professor level in the Department of Cell & Developmental Biology at SUNY Upstate Medical University in Syracuse. The Department is continuing a major expansion of its faculty. To complement and enhance the existing research interests, we will be recruiting into the general areas of cellular function and development. Areas of interest include, but are not limited to, cardiovascular development, cell differentiation, cell signaling, and developmental neurobiology. Substantial renovation and expansion of departmental research space and core facilities will continue in order to support the department's growth.

Candidates should have a Ph.D. and/or M.D. degree, and postdoctoral experience. Assistant Professors will be expected to develop an independent research program, while applicants at the Associate Professor level should have an established track record of research productivity and funding. Substantial startup packages and competitive salaries will be provided to all successful candidates. All Department faculty participate in the training and teaching of graduate and medical students.

Please submit CV, descriptions of research accomplishments, future plans for research and teaching interests as a single PDF file to **fontanek@upstate.edu** Please have three letters of recommendation sent to:

Dr. David Mitchell, Chair, Search Committee
Department of Cell & Developmental Biology
SUNY Upstate Medical University
750 East Adams Street, Syracuse, NY 13210
mitcheld@upstate.edu

For additional information, visit the department website
www.upstate.edu/cdb

State University of New York
Upstate Medical University
Formerly known as SUNY Health Science Center

SUNY Upstate Medical University is an AA/EEO/ADA employer committed to engaging excellence through diversity. Women and minorities are encouraged to apply.

Comparative Physiologist
University of Wyoming

The Department of Zoology and Physiology at the University of Wyoming invites applications for a full-time, nine-month, tenure-track **FACULTY POSITION**, starting August 2008, at the rank of Assistant Professor. Exceptional candidates may be considered at a higher level. We seek an individual interested in comparative, ecological, evolutionary and/or integrative aspects of physiology who uses molecular approaches to address physiological questions at the organismal level in natural systems, but encourage applicants with other backgrounds. The candidate must have a Ph.D. and a strong research record. The successful candidate will teach in our Department's physiology program. Departmental research strengths include ecology, wildlife/fisheries, neuroscience, and physiology.

Interested applicants should send a curriculum vitae, a statement of research and teaching interests, three publications, and three letters of recommendation to: **Physiology Search Committee, Dept. of Zoology and Physiology, Dept 3166, 1000 E University Avenue, Laramie, WY 82071. Fax: 307-766-5625. Website: http://uwyo.edu/Zoology; email: zprequest@uwyo.edu**. Review of applications will begin in **December 2007**.

The University of Wyoming is a Carnegie Foundation Research/Doctoral Extensive Institution, and is an AA/EEO Employer.

KU THE UNIVERSITY OF KANSAS
Faculty/Scientist Position in Global Biodiversity Modeling

The Department of Ecology and Evolutionary Biology (EEB) and Biodiversity Research Center (BRC) at the University of Kansas invite applications for a tenure-track position (open rank) in global biodiversity modeling as a joint Professor (EEB) and Scientist (BRC) beginning August 18, 2008, January 1, 2009, or negotiable. The successful candidate will maintain a strong, extramurally funded research program, teach undergraduate and graduate courses in ecology and areas of expertise, mentor graduate and undergraduate student research, collaborate widely, and contribute to service activities in EEB, BRC, the University, and the national and international scientific community. **Duties:** Conduct an active research program in biodiversity modeling and biodiversity informatics, emphasizing ecological and biogeographic contexts. Applicants at senior level must show evidence of research leadership in areas of biodiversity modeling, biodiversity informatics, and global biodiversity policy, including established record of publications and funding. A portion of the candidate's future research must be relevant to the North American Great Plains ecosystems with initial focus on the goals of the KS NSF/EPSCoR grant for eco-forecasting across the Kansas River basin; teach undergraduate and graduate courses in biology and related areas of expertise; mentor graduate and undergraduate student education and research; interact and collaborate with colleagues in biology and other disciplines; and contribute to the service activities in EEB, BRC, the University, and the scientific community. **Required Qualifications:** Ph.D. near completion, or terminal degree in Ecology and Evolutionary Biology or a related discipline by start date of appointment. Ph.D. is required within 12 months of the appointment start date; Evidence of a strong background in biodiversity modeling and biodiversity informatics; Demonstrated excellence in research evidenced by peer-reviewed publications; Commitment to education of undergraduate and graduate students and to service as documented by teaching experience or statement of teaching philosophy and plans; Commitment to seeking extramural research funding, evidenced by past grant success or detailed future plans for grant proposals; Women, minorities, and candidates who will contribute to the climate of diversity in the College, including diversity of scholarly approaches, are especially encouraged to apply. (For senior faculty/scientist, evidence of research leadership in the areas of biodiversity modeling and biodiversity informatics as demonstrated by track-record of publications and funding and eligibility for appointment with tenure at the Associate/Full Professor and Associate/Senior Scientist levels are required). For a complete position announcement and requirements, please refer to **http:// www.clas.ku.edu To Apply:** Submit curriculum vitae (with e-mail address), reprints of key papers, statements of current and future research plans and teaching philosophy that includes course-development interests, and have at least 3 letters of recommendation sent to: **Dorothy Johanning, University of Kansas, Department of Ecology and Evolutionary Biology, 1200 Sunnyside Avenue (Haworth Hall), Lawrence, KS 66045-7534; e-mail: jdorothy@ku.edu** Review of applications begins 15 October 2007, and continues until the position is filled. For more information visit **http://www.ku.edu/~eeb**

EO/AA Employer.

UNIVERSITY OF MASSACHUSETTS AMHERST
GLUCKSTERN PROFESSORSHIP

The Physics Department at the University of Massachusetts Amherst seeks a dynamic faculty member at the associate or full professor level with an outstanding record of research accomplishments, in experiment or theory, to fill the endowed Robert L. Gluckstern Distinguished Professorship in Physics. The Physics Department anticipates substantial new hiring in several areas over the next five years and our goal is for the holder of the Gluckstern Professorship to help the department to move in new directions. Although the position is open to all subfields of physics, we plan a major expansion in the area of biological physics during the next several years and one priority is to hire a leader in this field, who will help us to build an internationally recognized program. Communications from established scientists will be held in confidence and no references will be sought without approval. Applicants should send a vitae, bibliography, and a brief summary of research plans and teaching philosophy, and the names of five references to: **Gluckstern Faculty Search, Department of Physics – LGRT 1126, 710 No. Pleasant St., University of Massachusetts, Amherst, MA 01003**. Priority deadline is **November 9, 2007**; however, applications will be accepted until the position is filled. *The University of Massachusetts is an AA/EO Employer, and is aggressive in its efforts to hire candidates who will enhance the diversity and gender balance of the faculty in the sciences. We strongly encourage women and members of minority groups to apply.*

UNIVERSITY of ROCHESTER
Genomics and Systems Biology, Four Faculty Positions

To promote innovative and integrative research in life sciences and biomedicine, the University of Rochester announces an interdepartmental Initiative in Genomics and Systems Biology. This year, as part of the initiative, we will recruit four tenure-track faculty members at any level with expertise in the areas of genome biology, bioinformatics and proteomics. The successful candidates will benefit from a multidisciplinary research community, a vibrant graduate program and state of the art infrastructure and core facilities at the University of Rochester.

The Dept. of Biology in Arts, Sciences, and Engineering (**www.rochester.edu/College/BIO**) and the Dept. of Biomedical Genetics at the University of Rochester Medical Center (**www.urmc.rochester.edu/Aab/bg/**) will each fill two positions.

1. Functional Genomics/Systems Biology: *Department of Biology*. This position is for a scientist who studies basic problems in biology at a genomic or systems level. All qualified candidates will be considered. Those candidates working in the areas of Cell or Developmental Biology and Structural, Functional, or Computational Genomics are particularly encouraged.

2. Evolutionary/Comparative Genomics: *Department of Biology*. This position is for a scientist with research interests in genomic diversity within and between species. Research areas may include phylogenomics, genome-scale analyses of population variation, and the evolution of gene structure and function, gene networks, gene regulation, and non-coding DNA.

3. Complex Disease Genetics and Bioinformatics: *Department of Biomedical Genetics*. The successful candidate will use quantitative trait genetics, transcriptome analysis, large scale sequencing or other whole-genome approaches in conjunction with bioinformatics to pursue research in an area that matches the scope of scientific interests in the Department of Biomedical Genetics: Cancer, Disease Models, Signal Transduction, Stem Cell Biology, Neural Cell Function.

4. Systems Biology & Biological Modeling: *Department of Biomedical Genetics*. The successful candidate will apply advanced modeling and experimental techniques to pursue research in an area that matches the scope of scientific interests in the Department of Biomedical Genetics: Cancer, Disease Models, Signal Transduction, Stem Cell Biology, Neural Cell Function.

Candidates with a strong record of accomplishment should indicate Position Number and submit a CV, statement of research interests/plans, pdfs of two publications, and arrange to have three letters of recommendation sent to: **Gensys@ur.rochester.edu**. Review of applications will start **October 15, 2007**.

The University of Rochester is an Equal Opportunity Employer and has a strong commitment to diversity and actively encourages applications from candidates from groups underrepresented in higher education.

UNCCHARLOTTE

THE UNIVERSITY OF NORTH CAROLINA AT CHARLOTTE

TENURE-TRACK FACULTY POSITION STATISTICAL GENETICS

BIOINFORMATICS RESEARCH CENTER

The Bioinformatics Research Center at the University of North Carolina at Charlotte is seeking qualified applicants at all levels for a tenure-track faculty position in Statistical Genetics. We are especially interested in applicants with experience in the modeling of genome evolution, the application of phylogenetics to molecular evolution, the study of genetic variation at the population level, and whole-genome association studies, in particular those that integrate multiple molecular data types. Preference will be given to applicants with strong theoretical/method development interests. Our Center offers ample opportunities for collaborations that incorporate wet-lab activities both within the University and at neighboring clinical and biotechnology centers.

The successful applicant will be expected to develop a program of original research supported by external funding and to develop and teach graduate core courses in Statistics and Numerical Methods. Successful candidates must hold a Ph.D. in Bioinformatics, Genetics, Statistics, Biology, or a related field and have post-doctoral training.

Applications must be submitted online (position number **1842**) at **http://jobs.uncc.edu** and should include vitae, at least three references, and a letter of interest. We are unable to consider applications submitted by mail or e-mail. For full consideration, your application should be received by **October 15, 2007**, however, the position will remain open until filled. For additional information, please visit our website at **www.bioinformatics.uncc.edu**.

The University of North Carolina at Charlotte is an EOE/AA Employer.

UNCCHARLOTTE

THE UNIVERSITY OF NORTH CAROLINA AT CHARLOTTE

TENURE-TRACK FACULTY POSITIONS

BIOINFORMATICS RESEARCH CENTER

The Bioinformatics Research Center at UNC-Charlotte is seeking two tenure-track faculty with research interests in the application of post-genomic methods to personalized nutrition, crop development or food technology. All academic ranks will be considered. We are especially interested in applicants with experience in the development of novel computational techniques for the analysis of data from cutting edge technologies such as proteomics, metabolomics and lipidomics. The successful candidate will be expected to develop an independent externally funded research program, teach in our bioinformatics program, and collaborate with scientists of the DH Murdoch Research Institute at the North Carolina Research Campus (NCRC). The NCRC is a $1.5B, 350-acre biotechnology research park 18 miles north of the UNC-Charlotte campus offering world-class instrumentation and an unparalleled intellectual environment focused on human nutrition. The NCRC will be home to the research programs of a large number of private biotechnology companies, as well as those of at least six NC research universities and several health care organizations.

Successful candidates must hold a doctorate and have post-doctoral training in an appropriate field. Applications must be submitted online (position numbers **4367** and **4363**) at **http://jobs.uncc.edu** and should include vitae, at least three references, and a letter of interest. We are unable to consider applications submitted by mail or e-mail. For full consideration, your application should be received by **October 15, 2007**; however, the positions will remain open until filled. For additional information, please visit our website at **www.bioinformatics.uncc.edu**.

The University of North Carolina at Charlotte is an EOE/AA Employer.

University of Michigan Medical School

Department of Human Genetics

The University of Michigan Department of Human Genetics is recruiting faculty at the rank of **ASSISTANT PROFESSOR** with research interests in genetics and genomics. New faculty will join an active and growing program that includes molecular, developmental, population and statistical geneticists working with model organisms, patients, and populations.

Please apply by November 1 through the Department of Human Genetics web site at (http://www.hg.med.umich.edu/hr/). A curriculum vitae, description of current and future research, and three letters of recommendation should all be submitted through the web site. Correspondence should be addressed to:

Dr. Sally Camper, Chair
Department of Human Genetics
University of Michigan Medical School
4909 Buhl Bldg., 1241 Catherine St.
Ann Arbor, MI 48109-0618

Applications must be complete by 5:00 p.m. EDT on the November 1, 2007 deadline.

The University of Michigan is an Affirmative Action/Equal Opportunity Employer.

http://www.hg.med.umich.edu/

University of Michigan Medical School

Center for Genetics in Health and Medicine

The University of Michigan Department of Human Genetics is recruiting a faculty member to fill an **ENDOWED CHAIR** in the newly established, interdepartmental **Center for Genetics in Health and Medicine (CGHM)**. A basic science faculty appointment is available in the Department of Human Genetics. A physician-scientist active in patient care and research will hold a joint appointment in the appropriate clinical department. The Center's mission is to develop and support an interactive community of faculty in the basic and clinical sciences who will develop new research opportunities that integrate modern genetics research with clinical and public health activities.

Please apply by November 1 through the CGHM web site at (http://www.cghm.med.umich.edu/hr/). A curriculum vitae, description of current and future research, and three letters of recommendation should all be submitted through the web site. Correspondence should be addressed to:

Dr. Sally Camper, Chair
Department of Human Genetics
University of Michigan Medical School
4909 Buhl Bldg., 1241 Catherine St.
Ann Arbor, MI 48109-0618

Applications must be complete by 5:00 p.m. EDT on the November 1, 2007 deadline.

The University of Michigan is an Affirmative Action/Equal Opportunity Employer.

http://www.hg.med.umich.edu/

COLLEGE OF MEDICINE
THE UNIVERSITY OF TOLEDO

Faculty Position Cancer Biology

Applications are invited for a tenure-track position at the Assistant Professor level. Exceptional candidates will be considered for appointment at higher rank. We seek scientists working at the cellular, molecular or genetic levels on projects related to the causes, progression, diagnosis or treatment of cancer. Appointment will be in the Dept. of Biochemistry and Cancer Biology, with the possibility of a joint appointment in a clinical department for applicants doing translational research. Cancer research has been targeted for strategic emphasis, and excellent facilities, start-up packages, and collaborative opportunities are available. Research areas currently represented in the department include signal transduction, protein trafficking, DNA damage/repair, development of gene therapy vectors, and regulation of genes involved in cell growth, cell differentiation, and programmed cell death. Applicants should have a Ph.D. or M.D. degree with substantial postdoctoral research accomplishments. Successful candidates will be expected to develop or have extramural funding for their research program and be able to participate in the educational missions of the medical and graduate colleges.

Applications should include: a CV, description of research plans, copies of selected publications, and contact information for three references. Materials may be sent via regular mail or e-mail (PDF format) to:

Cancer Biology Search Committee
c/o Jenifer Zak
Department of Biochemistry and Cancer Biology
University of Toledo Health Science Campus - Mail Stop #1010
(formerly Medical University of Ohio)
3000 Arlington Ave.
Toledo, OH 43614
jenifer.zak@utoledo.edu

University of Toledo is committed to diversity and equal opportunity. Applications from women and minority candidates are strongly encouraged.

UNIVERSITY OF MINNESOTA

Department of Biochemistry, Molecular Biology and Biophysics and Cancer Center Tenure-Track Assistant Professor

The Department of Biochemistry, Molecular Biology and Biophysics in conjunction with the University of Minnesota Cancer Center (a NCI-designated Comprehensive Cancer Center) announces an opening for a tenure-track Assistant Professor. Candidates with interests that include fundamental processes such as chromatin organization, transcription and signaling as well as molecular mechanisms of cancer are particularly encouraged to apply. For more details about the Department and Center please consult: **http://cbs.umn.edu/BMBB/** and **http://www.cancer.umn.edu**.

The successful candidate will be expected to develop a strong, externally funded research program and contribute to the undergraduate, graduate and professional teaching programs of the Department. All candidates must have a Ph.D. and/or MD degree. Desired experience includes at least two years of postdoctoral experience and a strong publication record.

We will begin reviewing applications on **October 1, 2007** and applications will be accepted until the position is filled. Please apply online at **employment.umn.edu**, click on "Search Postings" and enter **150802** into the requisition number field. Please attach curriculum vitae and a brief statement of current and future research. Three letters of recommendation that consider both research and teaching potential should be sent to the: **Faculty Search Committee, c/o Ms. Ann Johnson, Department of Biochemistry, Molecular Biology and Biophysics, University of Minnesota, 6-155 Jackson Hall, 321 Church Street S.E., Minneapolis, MN 55455** or as an attachment to **swans143@umn.edu**.

The University of Minnesota is an Equal Opportunity Educator and Employer.

UNIVERSITY of MARYLAND 1807 200 Years SCHOOL of MEDICINE

Neurobiology Faculty Positions University of Maryland School of Medicine Baltimore, Maryland

The Department of Anatomy and Neurobiology (**http://neurobiology.umaryland.edu**) is recruiting tenured/tenure-track faculty positions in Neuroscience. We are interested in candidates who use multidisciplinary approaches to understand the function or plasticity of the nervous system. Of particular interest are candidates that complement existing strengths in the Department, including sensory, systems, molecular and developmental neuroscience. Candidates should have a strong history of scholarly activity and preference will be given to those with an independent funded research program.

The Department contains new, state-of-the-art laboratories and core facilities. We offer an outstanding intellectual and collaborative environment with highly competitive salary and recruitment packages. All department faculty are members of the Graduate Program in Life Sciences and the interdisciplinary Program in Neuroscience (**http://neuroscience.umaryland.edu**).

Candidates should submit the following as PDF files to **facsearch@umaryland.edu**: (1) detailed curriculum vitae, (2) statement of research interests and goals, and (3) names and contact information for three to five references. Applications should be addressed to the attention of: **Professor Reba Erzurumlu**, Chair, Faculty Search Committee.

UCLA

PHYSIOLOGY UCLA Assistant Professor

The **Department of Physiology** at the **David Geffen School of Medicine at UCLA** invites applications for a tenure track faculty position, preferably at the level of Assistant Professor.

We are especially interested in candidates using molecular physiological approaches such as functional genomics, proteomics, molecular imaging, or systems biology. Areas of departmental strength include molecular biophysics, neuroscience, and cardiovascular research, and candidates in these disciplines are encouraged to apply. However, we will consider applicants in all areas of modern physiology. Areas in which we might hope to expand include renal and respiratory physiology. Candidates are expected to have a strong background in cellular and molecular biology and a demonstrated interest in addressing fundamental physiological problems.

The successful candidate will be expected to develop an independent research program and participate in the teaching mission of the Department.

Interested applicants should email their curriculum vitae, a letter with a statement of research interests and career goals, and the names of three references to **Ms. Debra Moorehead** at **PhysiologySearch@mednet.ucla.edu**. Applicants should also arrange for three letters of reference to be sent to Ms. Moorehead at the same email address.

UCLA is an Affirmative Action/Equal Opportunity Employer. Women and minorities are encouraged to apply.

UNIVERSITY OF Cincinnati

Department of Genome Science
The University of Cincinnati College of Medicine

The University of Cincinnati College of Medicine seeks applications and nominations for the position of Professor and Chair, Department of Genome Science. The selected candidate will lead a significant expansion in the Department by building on existing strengths that include (i) well-funded faculty research programs in the genetics, signaling and metabolic aspects of cancer; (ii) state-of-the-art research space encompassing more than 50,000 square feet of laboratories; (iii) cutting-edge, onsite core facilities, such as proteomics, protein production, vivarium, mouse metabolic phenotyping, zebra fish aquaculture, *Drosophila* culture, and specialized equipment and personnel for high-throughput drug screening and drug discovery; and (iv) an interdepartmental graduate cancer biology training program.

Qualified candidates must hold a Ph.D., M.D. or M.D./Ph.D. degree and demonstrate ongoing success in research endeavors through a robust record of funding and publications. The research expertise should include, but is not limited to, cancer cell biology and cancer metabolism. Strong leadership in the academic community is essential.

Review of CVs will commence upon receipt and continue until the position is filled. Interested candidates should submit a comprehensive curriculum vitae and contact information for three references to: **Peter Stambrook, Ph.D., Search Committee Chair, c/o The Office of Faculty Affairs, The University of Cincinnati Academic Health Center, Eden Avenue & Albert Sabin Way, Health Professions Building/Room 161, Cincinnati, Ohio 45267-0554, Attention: Genome Science Chair** Or Email: **Patricia.Runtz@uc.edu.**

The University of Cincinnati is an Affirmative Action/Equal Opportunity Employer. Women, minorities, disabled persons, Vietnam era and disabled veterans are encouraged to apply. The Academic Health Center is a smoke-free work environment.

Stem Cells and Parkinson's Disease
University of Colorado Health Sciences Center
Denver, Colorado

The Stem Cell Biology Program, the Neurotransplantation Program for Parkinson's Disease, and the Division of Clinical Pharmacology at the University of Colorado Health Sciences Center seek a stem cell biologist with M.D., Ph.D., or M.D./Ph.D. degrees and appropriate background for a tenure-eligible position at an open rank. Some preference will be given to those with physician training. Applicants should have a strong record of research for their career stage. Successful candidates will be expected to develop an independent research program using stem cells to pursue the cause and treatment of Parkinson's disease. As faculty, they will be expected to participate in teaching of graduate and medical students.

The University of Colorado has a long record of innovative research in Parkinson's disease including the first transplant of human fetal dopamine cells in the United States in 1988. There are 12 faculty whose research interests focus on Parkinson's disease. They represent clinical and basic research departments in the School of Medicine, the School of Pharmacy and the Neuroscience Program. The Stem Cell Biology Program at the Health Sciences Center is headed by **Dennis Roop, Ph.D.** Its goals are to foster stem cell research across disciplines, providing resources and core facilities to make collaborative research successful.

Candidates should send curriculum vitae, a one page summary of research goals, and the names and contact information for three references to: **Curt R. Freed, M.D., Director, Neurotransplantation Program for Parkinson's Disease and Head, Division of Clinical Pharmacology, University of Colorado Health Sciences Center, Box C237, 4200 E. Ninth Ave., Denver, CO 80262; email: Curt.Freed@UCHSC.edu.**

The University of Colorado is an Affirmative Action/Equal Opportunity Employer. Women and minorities are encouraged to apply.

Assistant Professor Positions
Department of Molecular and Cellular Biology
Harvard University

As part of a broad expansion in the Life Sciences at Harvard University, the Department of Molecular and Cellular Biology seeks applications for tenure-track faculty positions. Our department covers a broad range of topics, including molecular biology, cellular biology, developmental biology, neurobiology, molecular evolution, systems biology, biochemistry, and structural biology, and provides access to state of the art animal facilities (mouse, zebrafish, Xenopus, Drosophila) and core facilities (imaging, proteomics, genomics, bioinformatics).

We strongly encourage applications from women and minority candidates. Applications should include: curriculum vitae, reprints of publications, and a statement of present and future research plans (1-3 pages). Complete applications and three letters of recommendation, solicited by the applicant, should be received not later than **3 November 2007**.

Submit applications to:
http://www.mcb.harvard.edu/Jobs/Faculty

For information contact **J. Blackbourn**/MCB Search Committee, **juliab@mcb.harvard.edu**, Department of Molecular and Cellular Biology, Harvard University

Harvard is an Affirmative Action/Equal Opportunity Employer.

www.mcb.harvard.edu

Johns Hopkins Medical Institutions
Tenure-Track Positions

Influenza and Respiratory Virus Translational Research

Human Immunology, Vaccinology, Pharmacology

The Division of Infectious Diseases of the Johns Hopkins School of Medicine is recruiting 1-2 faculty at the Assistant or Associate Professor level to contribute to an emerging institutional Respiratory Viruses Program. Our focus is on persons with proven capabilities to conduct independent research on respiratory infections, especially investigations that contribute to the prevention or treatment of influenza in humans. This recruitment contributes to expanding programs in influenza virology, structural biology, and vaccine testing. Emphasis will be given to researchers with complementary research such as in molecular biology of viral replication, host virus interactions, and quantitative analysis of viral dynamics.

Candidates must have earned an MD and/or PhD degree and have a record of acquiring research funding and producing outstanding scholarship. Salary and resources will match experience.

Candidates should provide a curriculum vitae, a one-page statement of career interest, and 3 professional references to: **Dr. David Thomas, Chief Infectious Diseases, Johns Hopkins School of Medicine, Suite 437 1830 Monument Street, Baltimore, Maryland 21205** or by email care of Nadia Hay **nhay@jhmi.edu**. Application review will begin in Fall 2007.

Johns Hopkins is an Equal Opportunity Employer.

SAINT MARY'S COLLEGE *of California*

Saint Mary's College invites applications for two full-time, tenure track Assistant Professors of Biology, both beginning Fall 2008:

- **Anatomy & Physiology**
- **Cell & Molecular Biology**

Teaching responsibilities will consist of upper-division and lower division courses. Additional courses in the candidate's area of expertise can be taught on a rotating basis.

A Ph.D. or other terminal degree in an area of expertise consistent with teaching responsibilities along with a record of teaching excellence, evidence of research trajectory, and publication in the field is required. Salary is competitive with excellent benefits package. Please visit our website at **www.stmarys-ca.edu** for complete job details and an online application.

To apply, submit a letter of interest, resume, on-line application and the names of three (3) professional references. Finalists will be expected to sign a consent authorizing a broader inquiry. Please forward all application materials to:

Gerard M. Capriulo, Ph.D. Fletcher Jones Professor of Biology & Chair, Biology Department, Saint Mary's College of California, PO Box 4507, Moraga, CA 94575.

Position is open until filled, and review of application materials will begin immediately.

An Equal Opportunity Employer

Faculty Positions

Yale Stem Cell Center

Yale University School of Medicine

The newly established Yale Stem Cell Center invites applications for faculty positions at the rank of Assistant, Associate, or Full Professor. Rank and tenure will be commensurate with experience. Applicants should have a Ph.D. and/or M.D. degree. Each successful candidate will be expected to develop a vigorous, externally funded research program on fundamental questions related to the biology of embryonic or adult stem cells. Investigators will join a vibrant stem cell research community at Yale with over 40 labs working on various aspects of stem cell biology and medicine, and will have opportunities to compete for Connecticut State funding for stem cell research, including research on non-federally approved human embryonic stem cell lines. Investigators will also contribute to teaching graduate and/or medical students as well as shaping stem cell research at Yale.

Applicants should mail a three-page research statement and CV, and arrange to have three reference letters sent to:

Haifan Lin, Ph.D., c/o Kristin Dugan
Director's Office, Yale Stem Cell Center
P.O. Box 208073, Yale University School of Medicine
10 Amistad Street, New Haven CT 06509

Application deadline is **December 15, 2007**. Follow-up inquiries should be sent to: **kristin.dugan@yale.edu**.

Yale is an Affirmative Action/Equal Opportunity Employer.

Center for Sensory Biology
Johns Hopkins University

The **Institute for Basic Biomedical Sciences** at **The JHU School of Medicine** has initiated a major initiative to recruit new faculty and create cross-disciplinary and highly interactive research centers.

The **Center for Sensory Biology** seeks to understand the fundamental processes underlying the primary senses – vision, touch (including pain), chemosensation (taste and smell) and hearing. Research within the Center is based on the recognition that sensory systems use conserved biological processes for signaling, adaptation and modulation, and for protection from injury, environmental insult, and degeneration. The Center is recruiting new faculty interested in working on diverse sensory systems and applying new tools and experimental approaches in a collaborative, interactive and interdisciplinary environment. Faculty will reside in new laboratories in the existing Basic Science research complex and receive primary appointments in existing Departments within the School of Medicine.

Applicants should submit an application by January 15, 2008 via email (IBBScenters@jhmi.edu). Include a CV, research plan, names of three references and up to three publications (all in pdf format). Indicate **CSB** in the subject line.

The Johns Hopkins University is committed to diversity and equality in education and employment and encourages applicants from under-represented groups.

Assistant/Associate Professor
Division of Medical Genetics, Department of Medicine
University of Washington

The University of Washington invites applicants for a faculty position at the rank of Assistant/Associate Professor, without tenure (physician/scientist pathway, M.D.), or Research Assistant/Associate Professor (Ph.D.), in the Division of Medical Genetics, Department of Medicine. The successful candidate will be expected to develop an independent, externally funded research program related to the genetic/genomic basis of human disease. Candidates with a strong research background involving the identification and characterization of disease genes, or the application of genetic/genomic information toward the diagnosis or treatment of human disease, are especially encouraged to apply. The successful candidate will have opportunities to collaborate with other outstanding members of the faculty, and will have access to state-of-the-art research facilities and clinical research programs. University of Washington faculty engage in teaching, research and service.

The position will be open until **December 31, 2007**. Send CV to:

David W. Emery, Ph.D.
K236C, HSB
1705 NE Pacific Street
University of Washington
Seattle, WA 98195-7720

The University of Washington is an Affirmative Action, Equal Opportunity Employer. The University is building a culturally diverse faculty and staff and strongly encourages applications from women, minorities, individuals with disabilities and covered veterans.

IDI
Immune Disease Institute

Assistant Professor, Structural Biology
Harvard Medical School
Immune Disease Institute

As a part of the Immune Disease Institute (IDI, formerly CBRI) Longwood Consolidation and a new building project to be completed in mid 2008, we are recruiting tenure track faculty at the rank of Assistant Professor in partnership with the Department of Biological Chemistry and Molecular Pharmacology (BCMP) at Harvard Medical School. IDI is highly interactive and offers outstanding opportunities for collaboration and technical support. The successful candidate will be offered a competitive start-up package. He/she will direct an independent research laboratory at IDI, and his/her work will complement and enhance the efforts of our distinguished faculty in cell biology, immunology, inflammation, vascular biology, infectious disease and cancer.

We are seeking a candidate who integrates macromolecular structure and biological function, especially someone who works on fundamental problems involving signal transmission in extracellular and cytoplasmic environments and across cell membranes. Approaches using molecular dynamics and spectroscopy, including EPR, protein structure prediction and design, X-ray crystallography and innovative light microscopy will be of special interest. The new structural biology initiative at IDI will be able to draw on available resources such as the HMS Center for Molecular and Cellular Dynamics (CMCD).

Please forward a cover letter requesting consideration by the search committee, curriculum vitae, reprints of key publications, letters separately sent from three referees, and a two-page statement of research interests including previous contributions and future research plans, no later than **October 30, 2007** to: **Timothy A. Springer and Tomas L. Kirchhausen, Search Chairs, Immune Disease Institute (IDI), 200 Longwood Avenue, Boston, MA 02115; recruitment@idi.harvard.edu.**

IDI and Harvard Medical School are Affirmative Action/Equal Opportunity Employers. Women and minority candidates are strongly encouraged to apply.

FACULTY POSITION IN BIOCHEMISTRY/ENZYMOLOGY
University of California, Davis

The Section of Molecular and Cellular Biology (MCB) within the College of Biological Sciences at the University of California, Davis, invites applications for a tenure-track position at the **ASSISTANT PROFESSOR** level. Competitive candidates must have a Ph.D. (or equivalent). The department seeks to hire talented new faculty who will develop an outstanding research program in the area of **BIOCHEMISTRY/ENZYMOLOGY** while maintaining a strong commitment to excellence in formal instruction of this discipline at both the undergraduate and graduate levels. Building on our highly interactive and multi-disciplinary research environment, MCB is interested in recruiting biochemistry/enzymology candidates who will complement the existing strengths of the section.

Candidates should submit a curriculum vitae, a 1-2 page summary of research accomplishments, a 1-2 page description of future research plans, copies of one to three major publications, and a statement of teaching experience and/or interest online at **www.mcb.ucdavis.edu**. Candidates should also arrange for three letters of recommendation to be submitted online or sent by mail to: **Faculty Search Committee, Section of Molecular and Cellular Biology, One Shields Avenue, University of California, Davis, CA 95616**. This position is open until filled although to assure full consideration, complete applications should be received prior to **November 1, 2007**.

The Section encourages women and minorities to apply. The University of California, Davis, is an Equal Opportunity/ Affirmative Action Employer.

The UNIVERSITY OF CHICAGO

The Department of Neurobiology in collaboration with the new Neuroscience Institute seeks to recruit new tenure-track faculty. The search will target individuals studying cerebral cortex and/or CNS development.

Interested persons should send their application to: (via regular mail)

S. Murray Sherman, Chairman
Department of Neurobiology
The University of Chicago
947 East 58th Street
Chicago, IL 60637

or via e-mail with attachments:
jdegroot@bsd.uchicago.edu

The applications should include a cover letter, curriculum vitae, a statement of research objectives, and the names and contact information of three academic references. Applicants are also responsible for arranging to have the reference letters sent. Applications will be accepted until the positions are filled. Application review will begin **November 1, 2007**.

The University of Chicago is an Equal Opportunity/ Affirmative Action Employer.

THE UNIVERSITY OF NORTH CAROLINA AT CHARLOTTE seeks applications for a **TENURE TRACK FACULTY POSITION** in **BIOCHEMISTRY** at the **ASSISTANT OR ASSOCIATE PROFESSOR** level, to begin August 15, 2008.

Required qualifications include: a Ph.D. in chemistry; postdoctoral, industrial or academic experience; a commitment to excellence in teaching at the undergraduate and graduate levels (including courses in biochemistry); and a commitment to establishing a productive, externally funded research program. Requirements for the associate professor level position also include a record of teaching, research productivity and external funding appropriate to rank. We especially welcome applications from biochemists interested in developing collaborations through participation in any of several interdisciplinary programs on campus, including the Nanoscale Science Ph.D. program, the Interdisciplinary Ph.D. in Biology, the Bioinformatics Research Center, the Center for Biomedical Engineering Systems, the Center for Optoelectronics and Optical Communications, and the emerging Biophysics community. Significant opportunities are also available to collaborate with the local Carolinas Medical Center. A unique opportunity exists to network from the ground up with the nearby North Carolina Research Campus (**http://www.ncresearchcampus.net**), a $1 billion 350-acre biotechnology research park that will be home to the research programs of private biotechnology companies, six North Carolina research universities and several healthcare organizations.

Applications must be made electronically at **https://jobs.uncc.edu** and must include a CV, the names and contact information of three references, and statements on research plans and teaching interests and philosophy. Questions about the search may be directed to **Dr. Joanna K. Krueger**, Chair of the Biochemist Search Committee, **jkkruege@uncc.edu**. For full consideration, all application materials should be received by **November 1, 2007**. Review of applications will begin immediately and continue until the position is filled. Applicants may visit **www.chem.uncc.edu** for more detailed information. UNC Charlotte, a 22,000 student campus of the University of North Carolina system, is one of the largest and fastest growing research universities in the Southeast and is situated on a modern, attractive, thousand-acre campus.

UNC Charlotte's academic climate respects the dignity of all individuals and encourages diversity including but not limited to ability/ disability, age, culture, ethnicity, gender, language, race, religion, sexual orientation, and socio-economic status. The University of North Carolina at Charlotte is an EOE/AA Employer and an ADVANCE Institution.

FACULTY POSITIONS
DEPARTMENT OF BIOENGINEERING
UNIVERSITY OF CALIFORNIA, SAN DIEGO

The Department of Bioengineering in the Jacobs School of Engineering at the University of California, San Diego is inviting applications for one or more TENURE-TRACK or TENURED FACULTY POSITIONS at the Assistant Professor, Associate Professor or Full Professor levels. Successful applicants will be expected to teach undergraduate and graduate courses in Bioengineering and to establish a vigorous program of high-quality federally funded bioengineering research, particularly research that focuses on genome-scale or systems approaches to biological complexity, integration across multiple scales from molecule to organism, and/or applications relevant to regenerative medicine. Exceptional candidates in other areas may also be given consideration.

The Jacobs School of Engineering enjoys close collaborations with the UCSD School of Medicine and the Divisions of Biological and Physical Sciences. Qualified individuals may be eligible for joint appointments. The level of appointment will be based on experience and qualifications. Salary will be based on published UC pay scales. Applicants are asked to submit materials on-line at **http://www-bioeng.ucsd.edu/recruit/**. Please include a cover letter, *curriculum vitae* including a complete list of publications, samples of published research and teaching evaluations (if available), the names and contact information of five referees, a statement summarizing research interests and teaching experience, and any leadership activities or contributions to diversity. Please do not include your Social Security Number.

For inquiries, please contact: **Faculty Search Committee Chair, Department of Bioengineering, 9500 Gilman Drive, Mail Code 0412, La Jolla, CA 92093-0412**, or by email to **recruit@bioeng.ucsd.edu**. Review of applications will begin **October 01, 2007** and continue until the position or positions are filled. For applicants with interest in spousal/partner employment, please see the web site for the UCSD Partner Opportunities Program.

UCSD is an EO/AA Employer with a strong institutional commitment to excellence through diversity.

Karolinska Institutet

PROFESSOR IN MEDICAL PROTEOMICS

Karolinska Institutet invites applications for a position as professor in Medical Proteomics.

For further details please contact Professor Jesper Haeggström, phone: +46 8 524 876 12 , email: **Jesper.Haeggstrom@ki.se** or the SACO union representative Michael Fored, phone: +46 8 517 791 81,email: **Michael.Fored@ki.se**

Please state your qualifications in accordance with the Karolinska Institutet qualification portfolio available on the Web page http://info.ki.se

Deadline for applications is **October 10, 2007. Reference no 2285/ 07-221**, Registrar, Karolinska Institutet, SE-171 77 Stockholm, Sweden.

For the entire advertisement please look at **http://jobb.ki.se/internal/general/starteng.asp** E-mail: **Registrator@ki.se**

FACULTY POSITION
CENTER FOR MICROBIAL PATHOGENESIS

The CENTER FOR MICROBIAL PATHOGENESIS at Columbus Children's Research Institute, Columbus Children's Hospital, and the Department of Pediatrics, College of Medicine, The Ohio State University seek PhD, MD, or MD/PhD candidates for a tenure-track position at the Assistant Professor rank to develop and conduct an independent research program in the fields of cellular and molecular microbiology. One area of interest includes bacterial pathogens causing disease in the airway with a specific emphasis on understanding the molecular mechanisms by which respiratory tract pathogens resist effectors of innate immunity and other related essential survival strategies. Applicants must have independent funding. Research space is available within the Columbus Children's Research Institute. This recruitment is part of a larger multi-year planned expansion of research initiatives by the institution and includes the 2004 completion of a 160,000-square-foot five-story research building that houses 48 state-of-the-art laboratory modules. Additional research space is slated to open in 2008. The Institute is equipped with leading-edge assets to facilitate collaboration and success, including animal facilities in addition to DNA sequencing, flow cytometry, informatics, histopathology, transgenic, microarray, ES cell, and transgenic cores. Joint appointments within graduate departments of The Ohio State University are available.

For more information, please visit our website at **www.ccri.net**.

Address correspondence with three references and curriculum vitae to:

Lauren O. Bakaletz, Ph.D.
Director, Center for Microbial Pathogenesis
Columbus Children's Research Institute
700 Children's Drive, Rm. W591
Columbus, OH 43205
Phone: (614) 722-2915 FAX: (614) 722-2818
E-mail: bakaletl@ccri.net

The Ohio State University is an Equal Opportunity/ Affirmative Action Employer. Qualified women, minorities, Vietnam-era veterans, disabled veterans, and the disabled are encouraged to apply.

THE OHIO STATE UNIVERSITY

COLUMBUS Children's RESEARCH INSTITUTE

PURDUE UNIVERSITY

The Department of Biochemistry invites applications for ***two*** tenure track faculty positions (1 Assistant Professor and 1 Associate Professor) that focus on either of the following.

1) The enzymology or engineering of metabolic pathways with significant impact on disease. Areas of particular interest include diabetes, cardiovascular disease and obesity.
2) The pathways and enzymes relevant to biofuel production. Areas of interest include plant cell wall biosynthesis, polysaccharide hydrolysis, and microbial fermentation of sugars to biofuel.

The successful candidates will be expected to develop a nationally and internationally recognized research program, interact with scientifically diverse faculty across campus and demonstrate excellence in teaching.

The Department of Biochemistry is part of a large and vibrant life science community at Purdue and our faculty participates in interdisciplinary programs in cancer, biophysics, genetics, plant biology and neuroscience. Support facilities are available for genomic analysis, metabolomics, protein mass spectrometry, NMR, X-ray crystallography, image analysis, computation, and transgenic animal work. For more information about our department, see **www.biochem.purdue.edu**.

Applicants for assistant professor should have a Ph.D. or M.D., at least two years of post-doctoral experience or its equivalent, a strong publication record, the potential to develop a vigorous extramurally funded research program, and a commitment to research and teaching excellence. Candidates at the associate professor level also should have a track record of significant external funding. Applicants are asked to submit materials electronically to **biochem-search@purdue.edu**. Applications should include a cover letter, curriculum vitae, a two-page summary of research interests, a statement of teaching objectives/interests and the names and contact information of three references. Screening of applicants will begin **October 12, 2007** and continue until the positions are filled.

Purdue University is an Equal Opportunity/Equal Access/Affirmative Action Employer fully committed to achieving a diverse workforce. Women and individuals from underrepresented groups are encouraged to apply.

KU THE UNIVERSITY OF KANSAS

Faculty/Scientist Position in Ecosystem Scientist

The Department of Ecology and Evolutionary Biology (EEB) and the Kansas Biological Survey (KBS) at the University of Kansas (KU) invite applications for a tenure-track position in ecosystem ecology as a joint Assistant Professor (EEB) and Assistant Scientist (KBS) beginning August 2008 or January 2009. The successful candidate will maintain a strong, extramurally funded research program, teach undergraduate and graduate courses in ecology and areas of expertise, mentor graduate and undergraduate student research, collaborate widely, and contribute to service activities in EEB, KBS, the University, and national and international scientific community.

We seek candidates who will conduct research in terrestrial or aquatic ecology that emphasizes dynamic processes at the ecosystem, landscape, and/or global level, and who will develop and/or apply models as predictive and/or scaling tools in the context of environmental change. Examples of research areas could include, but are not limited to, biogeochemical fluxes, ecosystem energetics, organic matter processing, and/or the relationships between biodiversity and ecosystem function. A portion of the candidate's future research must be relevant to the North American Great Plains ecosystems with initial focus on the goals of the KS NSF/EPSCoR grant for eco-forecasting across the Kansas River basin.

Required Qualifications are: Ph.D. by date of appointment in an appropriate discipline; demonstrated excellence in ecosystem research (evidenced by peer-reviewed publications); commitment to service and to graduate and undergraduate student education (documented by teaching experience or statement of teaching philosophy and plans); commitment to seeking extramural research funds (evidenced by past grant success or detailed future plans for grant proposals); and willingness to contribute to the climate of scholarship and the diversity of thought and approaches at KU. Post-doctoral experience is preferred. For a complete position announcement and requirements, please refer to the KU College of Liberal Arts & Sciences website at **http://www.clas.ku.edu**

To Apply: Submit curriculum vitae, key reprints, statements of research plans and teaching philosophy with course-development interests, and have at least 3 letters of recommendation sent to: **Dorothy Johanning, University of Kansas, Department of Ecology and Evolutionary Biology, 1200 Sunnyside Avenue (Haworth Hall), Lawrence, KS 66045-7534; e-mail: jdorothy@ku.edu** Review of applications begins 15 October 2007, and continues until the position is filled. For more information visit **http://www.ku.edu/~eeb**

EO/AA Employer.

WORKING AT THE UNIVERSITY OF GENEVA

The FACULTY OF SCIENCE seeks an

ASSISTANT or ASSOCIATE or FULL PROFESSOR
in Plant Molecular Biology

(www.unige.ch/sciences/biologie/bioveg)

POST: Full-time research and teaching position in the general area of plant molecular biology. Special consideration given to scientists studying important biological problems using novel multidisciplinary approaches.

REQUIREMENTS: Ph.D. degree or equivalent. Experience in teaching and leading an independent research project.

STARTING DATE: 1st January 2008 at the earliest.

Candidate files must be addressed before **November 2nd, 2007** to : Décanat de la Faculté des sciences, 30, Quai Ernest Ansermet, CH-1211 Genève 4, from whom additional information can be obtained regarding the responsibilities of the post and other conditions.

The University of Geneva is an equal opportunity employer and encourages applications from female candidates.

UNIVERSITÉ DE GENÈVE

Tenure-Track Position Applied Physics – #07244

Located in Ithaca, N.Y., Cornell University is a bold, innovative, inclusive and dynamic teaching and research university where staff, faculty, and students alike are challenged to make an enduring contribution to the betterment of humanity.

The School of Applied and Engineering Physics at Cornell University is seeking applications for a tenure-track, assistant professor position. Consideration of applications for an associate or full professor level position may also be given to exceptionally well qualified individuals. Candidates must be able to demonstrate the ability to develop a highly successful independent research program in an area of applied physics and to participate effectively in the teaching of the applied physics curriculum at both the undergraduate and graduate level. Research areas of interest in this search include, but are not limited to, optics and photonics, biological physics, nanostructure science and technology, novel instrumentation methods, computational physics, and materials physics. Prospective candidates who wish to pursue interdisciplinary research efforts are strongly encouraged to apply. The successful applicant can expect a very competitive level of support for the start-up of a research program. Considerable institutional resources are available at Cornell that can strengthen this research program and support interdisciplinary and collaborative research ventures. The successful candidate can expect to benefit from association with one or more of Cornell's interdisciplinary research centers, national facilities, and national resources, listed at **http://www.engineering.cornell.edu/ research/research-centers/**

Applications consisting of a resume, a statement of teaching philosophy, a brief (3-page limit) statement of research interests, and the names and addresses of at least three references, should be submitted on-line at **http://fast.aep.cornell.edu/**.The application deadline is December 15, 2007. Interviewing will begin after January 1, 2008 and will continue until the position is filled.

Cornell University

Cornell University is an Affirmative Action/ Equal Opportunity Employer and Educator.

http://chronicle.com/jobs/profiles/2377.htm

University of Nebraska Lincoln — IANR

Professor and Chair
Department of Biochemistry
University of Nebraska-Lincoln

The University of Nebraska-Lincoln is seeking an individual with an outstanding research program and excellent interpersonal skills who can provide energetic and creative leadership for the research, teaching, and public service activities of its **Department of Biochemistry**. A competitive start-up package is available for this full time, 12-month appointment. The **Department of Biochemistry** is rapidly growing and includes 15 budgeted and 10 affiliated faculty members. The research programs in the **Department** are currently supported by annual grant and contract awards exceeding $5 million. The **Department** houses the NIH-funded Redox Biology Center and has established strengths in biomedical research, plant biochemistry, structural biology, bioinformatics, and classical enzymology. The **Department** is located in the state-of-the-art George W. Beadle Center, which is also the home of the NIH-funded Nebraska Center for Virology, the Plant Science Initiative, the Center for Biotechnology, and key core research facilities. To learn more about the **Department**, please visit the website **http://biochem.unl.edu**.

To apply for this position, access the web site **http://employment.unl.edu**. Search for position number **070695**. Complete the faculty academic administrative information form. Attach a letter of application, curriculum vitae, and the contact information for three professional references. Review of applications will begin on **October 19, 2007**, and continue until the position is filled.

The University of Nebraska is committed to a pluralistic campus community through Affirmative Action and Equal Opportunity and is responsive to the needs of dual career couples. We assure accommodation under the Americans with Disabilities Act; contact Linda Arnold at 402-472-3802 for assistance.

Immunology Faculty Position at the Sloan-Kettering Institute

The Immunology Program at the Sloan-Kettering Institute (SKI) is seeking innovative investigators for tenure-track positions at the Assistant, Associate, and Member levels who wish to address basic problems in immunology with possible relevance to cancer. Applicants should have a doctoral-level degree and the potential to develop a strong independent research program or a proven record of accomplishments, depending on the level of appointment. Qualified applicants with an M.D. degree may be offered a joint appointment in an appropriate department in Memorial Hospital. Candidates will join a faculty with a broad range of research interests, including transplantation, T and NK cell development and function, gene regulation, antigen presentation, infectious disease and tumor immunology. The program has recently moved into contiguous space on 3+ floors in a new 23 story laboratory building. Faculty will be eligible to hold graduate school appointments in the Gerstner Sloan-Kettering Graduate School of Biomedical Sciences, the Weill Graduate School of Medical Sciences of Cornell University, as well as the Tri-Institutional MD/PhD Training Program.

SKI offers a highly interactive, supportive and exciting research environment with programs in Immunology, Cancer Biology & Genetics, Cell Biology, Molecular Pharmacology & Chemistry, Molecular Biology, Developmental Biology, Computational Biology and Structural Biology, as well as unparalleled clinical programs in cancer research, treatment and prevention.

Candidates should e-mail their application, preferably in PDF format, to **immuno@mskcc.org.** The application should include a CV, a description of past research, a description of proposed research, and copies of three representative publications. Candidates should arrange to have three signed letters of reference sent by e-mail to immuno@mskcc.org or regular mail to: **Dr. James P. Allison, Chairman, Immunology Program, C/O Dwana Agosto, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, Box 494, New York, NY 10065.** Application Deadline: November 1, 2007. For more information please visit our website at www.ski.edu. For Questions please email **agostod@mskcc.org.** Memorial Sloan-Kettering Cancer Center is an affirmative action, equal opportunity employer.

Memorial Sloan-Kettering Cancer Center
The Best Cancer Care, Anywhere.
www.mskcc.org

Center for Learning and Memory
Institute for Neuroscience
The University of Texas at Austin

The Center for Learning and Memory at the University of Texas at Austin invites applications for a number of tenure track faculty positions at the **Assistant, Associate, and Full Professor levels**.

While the field of interest is open, we are particularly interested in candidates using genetic and molecular approaches to investigate plasticity, learning, and memory in mammals. Successful candidates will join an expanding and vibrant academic environment and will be expected to develop and maintain an active research program. Academic appointments will be made in the appropriate academic unit within the College of Natural Sciences, College of Arts and Sciences, School of Pharmacy, or School of Engineering. The positions will include highly competitive salary and start-up packages.

The University of Texas in Austin is involved in a major expansion of the Institute for Neuroscience, building upon a strong faculty base in Neurobiology, Psychology, Pharmacy, Computer Science, Integrative Biology, Biomedical Engineering, Physics, Chemistry, and the Institute of Cell and Molecular Biology. Successful candidates will have their laboratories in the new Neural and Molecular Sciences Building located in the heart of the beautiful UT campus.

Austin is located in the Texas hill country and is widely recognized as one of America's most beautiful and livable cities (see: **www.austintexas.org/home/** and **www.ci.austin.tx.us**).

Please send curriculum vitae, summary of research interests, and names of five references to: **Dr. Daniel Johnston, Director, Center for Learning and Memory, Institute for Neuroscience, The University of Texas at Austin, 1 University Station, C7000, Austin, TX 78712-0805.**

Homepage: **http://clm.utexas.edu/**

The University of Texas at Austin is an Equal Opportunity Employer. Qualified women and minorities are encouraged to apply; a background check will be conducted on applicants selected.

BCM
Baylor College of Medicine

The Department of Biochemistry and Molecular Biology invites applications for a tenure-track faculty position at the **ASSISTANT** or **ASSOCIATE PROFESSOR** rank. The Department maintains diverse areas of research with strengths in molecular genetics, developmental biology, cell biology, signal transduction, neurobiology, and structural biology. We are seeking outstanding candidates who are pursuing cutting-edge research in molecular, cell, or developmental biology. We are especially interested in the areas of genome instability, regulatory networks, membrane and organellar biology, and mouse models of human disease.

Our Department offers a collegial, collaborative environment and has a tradition of being very supportive of new faculty. Baylor College of Medicine is located in the heart of the Texas Medical Center and is affiliated with 11 educational institutions, including the University of Texas Medical School, The UT MD Anderson Cancer Center, and Rice University, to name a few. Academic rank and salary are commensurate with experience and qualifications. Candidates should send a cover letter, curriculum vitae, statement of research interests, and names and contact information for three references.

Applications may be submitted electronically to: BMBsearch@bcm.edu or by mail to: **Dr. John Wilson, BMB Faculty Search, Department of Biochemistry and Molecular Biology, Baylor College of Medicine, One Baylor Plaza, Houston, Texas, 77030**. The committee will review applications beginning **September 1, 2007**, and will continue until the position is filled.

Baylor College of Medicine is an Equal Opportunity Affirmative Action and Equal Access Employer.

KU THE UNIVERSITY OF KANSAS
Evolutionary Genomics Scientist

The Department of Ecology and Evolutionary Biology at the University of Kansas invites applications for a tenure-track faculty position at the Assistant Professor level. Position is expected to start August 18, 2008. The successful candidate will maintain a strong, extramurally funded research program, teach undergraduate and graduate courses in genetics and/or evolutionary biology and areas of expertise, mentor graduate and undergraduate student research, collaborate widely, and contribute to service activities of the department, the university, and the national/international scientific community. **Duties:** conduct experimental research in the field of evolutionary genomics. Preference will be given to candidates with a research program that (1) combines molecular and classical genetic approaches to study a genetically tractable organism, and (2) develops theory in relation to his/her experimental work. **Required qualifications:** Ph.D. or terminal degree in an appropriate field expected by start date of appointment; postdoctoral experience in genomics or a related field; demonstrated excellence in research in evolutionary genetics/genomics; commitment to service and to undergraduate and graduate student education; and commitment to seeking extramural research funding. Women, minorities, and candidates who will contribute to the climate of diversity in the College, including diversity of scholarly approaches, are especially encouraged to apply. For a complete position announcement and requirements, please see the KU College of Liberal Arts & Sciences website at **www.clas.ku.edu To apply:** submit curriculum vitae (with e-mail address), reprints of key papers, statements of current and future research plans and teaching philosophy that includes course-development interests, and have at least three letters of recommendation sent to: **Dorothy Johanning, Dept. of Ecology & Evolutionary Biology, University of Kansas, 1200 Sunnyside Ave., Lawrence, KS 66045-7534 (e-mail: jdorothy@ku.edu)**. Review of applications begins 15 October 2007 and continues until position is filled. For more information, visit **http://www.ku.edu/~eeb**

EO/AA Employer.

BCM
Baylor College of Medicine

Baylor College of Medicine seeks applications for a tenure-track or tenured faculty position in the Department of Biochemistry and Molecular Biology (**http://www.bcm.edu/biochem/**). We are especially interested in individuals with interdisciplinary research programs using and developing cutting edge technology in the areas of chemical biology, high-throughput screening, molecular biophysics, and molecular imaging. These research areas will complement existing strengths in the Department in structural and computational biology, molecular biophysics, proteomics, receptor structure/function, RNAi screening, and genetics of model organisms. The successful applicant will have the opportunity to participate in the highly interactive and collaborative research and training programs of the Gulf Coast Consortia, which include BCM, University of Texas Houston Medical School, M.D. Anderson Cancer Center, Rice University, the University of Houston, and University of Texas Medical Branch.

We offer competitive start-up and salary, commensurate with experience and qualifications. Candidates should submit electronic versions (PDF or Word files) of a cover letter, curriculum vitae, statement of research interests, and names and contact information for three references to **Dr. Theodore Wensel** at: **bmb-cb@bcm.edu**. The committee will review applications beginning **September 1, 2007**, and will continue until the position is filled.

Baylor College of Medicine is an Equal Opportunity Affirmative Action and Equal Access Employer.

NORTHWESTERN UNIVERSITY

The Department of Neurobiology and Physiology in the Weinberg College of Arts and Sciences seeks to recruit a new faculty member at the **Assistant Professor** level. Applicants holding a Ph.D or M.D. degree, and demonstrating an outstanding record of scientific achievement will be considered. We are interested in individuals whose research addresses fundamental issues in neuroscience and who show significant potential for innovation, scholarship, and commitment to excellence in research and teaching. Successful candidates will be expected to establish and maintain a high-profile research program attracting substantial extramural funding. The appointee will have access to state-of-the-art life science research support facilities and opportunities to interact with colleagues in the Institute for Complex Systems, Cognitive Neurology and Alzheimer's Disease Center, Center for Reproductive Science, Center for Sleep and Circadian Biology, Robert H. Lurie Comprehensive Cancer Center, and an interdepartmental neuroscience graduate program with over 150 faculty.

Applicants should submit a curriculum vitae and description of research plans to: **Search Committee Chair, Department of Neurobiology and Physiology, Northwestern University, 2205 Tech. Dr., Evanston, IL 60208 (www.northwestern.edu/neurobiology/).** Three letters of recommendation should be sent to the same address. Applications received by **November 15, 2007** will be ensured full consideration.

Northwestern University is an Affirmative Action/Equal Opportunity Employer. Women and minority candidates are encouraged to apply.

Tenure Track Faculty Positions in Developmental Biology

Sloan-Kettering Institute, Memorial Sloan-Kettering Cancer Center invites applications for junior tenure-track faculty positions in the Program in Developmental Biology. Successful candidates will carry out independent research programs addressing problems in any aspect of Developmental Biology. Topics of particular interest include stem cell biology, gametogenesis and genetic mechanisms in development. Sloan-Kettering Institute offers a highly interactive and exciting research environment with outstanding infrastructure and resources to support research (www.ski.edu). New faculty will be eligible to hold graduate school appointments in the Gerstner Sloan-Kettering Graduate School of Biomedical Sciences, the Weill Graduate School of Medical Sciences of Cornell University, as well as the Tri-Institutional MD/PhD Training Program.

Candidates should e-mail their application in PDF format to: **devbio@mskcc.org** by November 1, 2007. The application should include a Curriculum Vitae, a description of past research, a description of proposed research, and copies of three representative publications. Candidates should arrange to have three letters of reference sent by e-mail to: **devbio@mskcc.org** and by regular mail to: **Developmental Biology Search, c/o Ms. Tiffany Lennon, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, Box 135, New York, New York 10065.** The letters should arrive by November 1, 2007. Inquiries may be sent to Ms. Lennon at: **devbio@mskcc.org** or to Dr. Kathryn Anderson, Chair, Developmental Biology Program, Sloan-Kettering Institute. Memorial Sloan-Kettering Cancer Center is an Equal Opportunity Employer.

Memorial Sloan-Kettering Cancer Center
The Best Cancer Care, Anywhere.
www.mskcc.org

PURDUE UNIVERSITY

Faculty Positions
College of Science – Purdue University

As part of its strategic plan, the College of Science at Purdue is hiring faculty in several exciting areas, including core hires with the departments and interdisciplinary hires in thrust areas identified by the College. All hires will have a departmental home in one of the college's seven departments:

- Biological Sciences
- Chemistry
- Computer Science
- Earth and Atmospheric Sciences
- Mathematics
- Physics
- Statistics

Multidisciplinary hires may be joint between departments or with other colleges. Links to these departments and the application sites can be found on the College of Science hiring page:

http://www.science.purdue.edu/hiring/.

A Ph.D. in a field related to the position sought is required. The successful candidates will teach courses and conduct research in their area of specialty. Applications from outstanding candidates in all areas will be considered.

Purdue University is an Equal Opportunity/Equal Access/Affirmative Action Employer fully committed to achieving a diverse work force. Women and individuals in underrepresented groups are encouraged to apply.

FACULTY POSITIONS AT THE ROCKEFELLER UNIVERSITY

The Rockefeller University seeks exceptional, interactive, and creative scientists to join its faculty. We invite applications from outstanding candidates for tenure-track positions and also encourage tenured Professors to apply, provided that they are early on in their careers.

The Rockefeller University provides strong financial support for the research work of its faculty. The positions offer highly competitive salary, benefits and start-up funds, new or recently renovated laboratory space, access to numerous state-of-the-art core facilities and extensive opportunities for collaboration both within the University and with neighboring institutions. The University also provides very strong continuing support for research work beyond start-up, including full support for graduate students.

The University has a laboratory-based organization structure that fosters interdisciplinary research in the following areas:

- **Chemical Biology**
- **Evolution and Ecology**
- **Medical Sciences and Human Genetics**
- **Microbiology and Immunology**
- **Neurobiology**
- **Physics and Biology**
- **Physiology of Organisms**
- **Physiology of Single Cells**

Details about specific subjects of research can be found at: **http://www.rockefeller.edu/facultysearch.**

Applications are being accepted electronically through our **Online Application System** at **http://oas.rockefeller.edu.**

Applicants should follow the online application procedure which includes submitting the following:

- Curriculum Vitae with a publications list
- Statement of Research with a 2 page description of significant research accomplishments and a 2 page description of future research plans (4 pages maximum)
- Relevant publications (optional, maximum of 3)

If you have questions regarding submitting an application, please contact our Faculty Search Administrator at **facultysearch@rockefeller.edu.**

The deadline for receipt of applications is November 9, 2007. The search will be reopened in February, 2008 with a deadline of April 15, 2008.

The Rockefeller University is an Affirmative Action/Equal Opportunity/VEVRAA Employer and welcomes applications from women and under-represented minorities.

Center for Immunology and Microbial Disease Albany Medical College

Faculty Position

The Center for Immunology and Microbial Disease at Albany Medical College invites applications for a tenure-track faculty position from individuals who have a doctoral degree, postdoctoral experience, and demonstrated research productivity. Those with an interest in bacterial pathogenesis and host-pathogen interactions are particularly encouraged to apply. The successful candidate will be expected to establish an independent, extramurally funded research program and participate in the teaching of medical and graduate students. The basic science departments at Albany Medical College are organized as interdisciplinary research centers and the Center for Immunology and Microbial Disease has a focus on microbial pathogenesis and immune defense, particularly as related to biothreat agents and emerging infections. Faculty at the Albany Medical College receive competitive salaries, attractive start-up packages, and access to the Center's ABSL-3/BSL-3, Microbiology and Immunology Core Labs. In addition, we have established a close relationship with the New York State Department of Health Wadsworth Laboratories, providing a diverse environment that is rich in infectious disease expertise. Albany Medical College is located in a mid-sized city within the upstate New York Capital Region, and has easy access to Boston, New York City, and the Adirondack Mountains.

Applicants should send their curriculum vitae, a statement of research plans, and three letters of reference to: **Dennis W. Metzger, Ph.D., Professor, Theobald Smith Alumni Chair and Director, Center for Immunology and Microbial Disease, Albany Medical College, 47 New Scotland Avenue, MC-151, Albany, NY 12208.** For further information about the Center, visit **www.amc.edu/Academic/Research/imd.htm**.

An Equal Opportunity/Affirmative Action Employer. Women and minorities are encouraged to apply.

Wheaton College

for Christ and His Kingdom

Exercise Physiologist Position

The Applied Health Science Department of Wheaton College is searching for a full-time, tenure track faculty member with expertise in exercise physiology at the assistant or associate professor level. The person appointed will make a significant contribution to the department's academic and spiritual components. The person will be a well trained physiologist with the specialty of exercise along with a good biochemistry and metabolism background. This person must be able to engage students in the classroom setting and to mentor them in independent research projects. The teaching requirements include courses in Integrative Human Physiology, Physiology of Exercise, Cardiovascular Evaluation and Prescription, and general education classes in Wellness. The person will develop elective courses in his/her area of specialty. The department is focused on human health and lifestyle with most of its students pursuing careers in the health professions. A doctorate is required.

Deadline for applications is October 31, 2007

The appointment will begin July 1, 2008

Applicants should send curriculum vita and description of their teaching philosophy and research interests to: Dr. David Ianuzzo, Chair; Applied Health Science Department; Wheaton College; 501 College Avenue; Wheaton, IL 60187 or email **david.ianuzzo@wheaton.edu**

Additional application materials will be sent to eligible candidates.

Wheaton College is an evangelical Christian liberal arts college whose faculty members affirm a Statement of Faith and the moral and lifestyle expectations of our Community Covenant. The College complies with federal and state guidelines of nondiscrimination in employment; women and minorities are encouraged to apply.

ASSISTANT PROFESSOR IN NEUROSCIENCE

Applications are invited for a tenure-track Assistant Professor position in the Julius L. Chambers Biomedical/ Biotechnology Research Institute (BBRI) at North Carolina Central University (NCCU). The BBRI is a 40,000 sq ft state-of-the-art research institute, with research programs in neuroscience, cardiovascular and cancer biology. Research resources available at the BBRI include: genomics and bioinformatics core facilities; histopathology and imaging laboratories; a zebrafish core and a modern animal care and use facility. The proximity of NCCU/BBRI to the North Carolina Research Triangle Park and to collaborative colleges and universities will afford the candidate an unusually rich opportunity to develop joint programs in neuroscience that have a high probability for long-term success.

The successful candidate will be expected to: establish an extramurally funded research program that focuses on neurodegenerative diseases or CNS development; train graduate students in Neuroscience; and teach at the undergraduate and/or graduate level in Neuroscience. Preference will be given to individuals using mouse or zebrafish models to study the molecular mechanisms of neurodegenerative diseases. Applicants must hold a Ph.D. and/or M.D., and have a record of research productivity in Neuroscience.

Review of applicants will begin immediately and will continue until the position is filled. Applicants should submit curriculum vitae, a description of research interests, and contact information for three references to:

Ms. Connie Key
Julius L. Chambers Biomedical/Biotechnology Research Institute
North Carolina Central University
700 George Street
Durham, NC 27707

Email: chkey@nccu.edu

For more information about the BBRI and NCCU visit **http://www.nccu.edu/BBRI**.

North Carolina Central University is a constituent institution of the University of North Carolina System and an Equal Opportunity, Affirmative Action Employer. NCCU complies with the Immigration Reform and Control Act of 1986.

The Ohio State University Medical Center

Department of Physiology and Cell Biology Tenure Track Faculty Position

The Department of Physiology and Cell Biology at The Ohio State University invites applications for a tenure track appointment at the Assistant Professor level in cardiovascular cell and molecular physiology. We are especially seeking individuals performing cutting-edge research focused on cellular signaling pathways relevant to cardiac development, hypertrophy and heart failure. The appointment is to complement existing strengths in Cardiac Calcium homeostasis and muscle physiology. Exceptional candidates in any area of cell signaling will also be considered. The successful candidate will have an established externally funded research program or the ability to establish one. Faculty will also have the opportunity to collaborate with scientists in the Davis Heart and Lung Research Institute and other established research centers. Faculty will be expected to participate in the Departmental teaching activities as appropriate. Letters of application should clearly outline teaching and research interests along with Curriculum Vitae and a list of references.

Please apply for this position to: **Muthu Periasamy, Ph.D., Chair, Dept. Physiology and Cell Biology, The Ohio State University, 304 Hamilton Hall, Columbus, OH 43210-1218, periasamy.1@osu.edu**. See departmental website: **www.medicine.osu.edu/physiology**.

The Ohio State University is an Equal Opportunity/ Affirmative Action Employer.

DANA-FARBER CANCER INSTITUTE

Dedicated to Discovery...Committed to Care.

ASSISTANT PROFESSOR

(Tenure Track)

Metabolic Regulation

The Department of Cancer Biology at Dana-Farber Cancer Institute and the Department of Pathology at Harvard Medical School seek applicants for a tenure-track faculty position. We will consider outstanding applicants interested in any area of cellular and molecular biology, but we are particularly interested in candidates working in the area of regulation of energy homeostasis as it relates to chronic diseases such as cancer, diabetes, aging and neurodegenerative diseases. The ideal candidate will be capable of working at the cell and molecular level, but will also have experience with in vivo model systems. The successful applicant will be expected to develop a strong, independently funded research program and to participate in the teaching mission of the Institute and Harvard Medical School. Candidates must hold a Ph.D. and/or M.D. degree and have a strong record of research accomplishments. Applications from women and minority candidates are encouraged.

Candidates should submit a curriculum vitae including a full list of publications, a brief statement of previous contributions and future research plans as well as the names and contact information of four references to:

Faculty Search Committee
c/o Deborah Goff
Dana-Farber Cancer Institute
Room SM1068, 44 Binney Street, Boston, MA 02115
E-mail: deborah_goff@dfci.harvard.edu

HARVARD MEDICAL SCHOOL

Applications must be received by November 1, 2007

The Dana-Farber Cancer Institute is an Equal Opportunity Employer.

SHARE THE VISION. FIND THE CURE

HARVARD MEDICAL SCHOOL PARTNERS HEALTHCARE SYSTEM

FACULTY POSITIONS IN GENETICS AND GENOMICS

The Harvard Medical School - Partners HealthCare Center for Genetics and Genomics (HPCGG) is seeking exceptional candidates to lead research programs in human genetics and genomics. Successful candidates will be appointed at the level of tenure-track Assistant Professor. For more information, please visit our website at www.hpcgg.org

Applicants should electronically submit a curriculum vitae, a brief (500 word) statement of current and future research directions, and have three letters of reference sent on their behalf to:

Christine Seidman, M.D.
Associate Director, HPCGG
c/o Andrea Wald McDonald
77 Avenue Louis Pasteur, NRB 250
Boston, MA 02115

Email to: **awaldmcdonald@partners.org**

The application deadline is **December 1, 2007**.

Women and minority candidates are encouraged to apply. Harvard Medical School and Brigham and Women's Hospital are Equal Opportunity/Affirmative Action Employers.

UNIVERSITY OF Miami

Aresty Endowed Chair in Tropical Biology

The Department of Biology of the University of Miami seeks a distinguished scientist for the Aresty Endowed Chair in Tropical Biology. The appointment will be made at the associate professor or professor rank. The chair holder must be renowned for tropical terrestrial research with animals, and will contribute to the department's focus on ecology and evolution in tropical systems. Field work should be an integral component of the candidate's research. We seek an excellent teacher who will offer both undergraduate and graduate courses including an undergraduate field course, off campus, in the tropics.

Applicants should send electronically a curriculum vitae, statements of research and teaching interests, and contact information for three references to:

Aresty_Chair@bio.miami.edu.

The University of Miami is committed to increasing the representation of women and minorities in its faculty, and encourages applications from such candidates.

Faculty Position Cell Biology Program Sloan-Kettering Institute

The Cell Biology Program, Sloan-Kettering Institute (www.ski.edu) has initiated a search for tenure-track faculty members. We are interested in outstanding individuals who have the potential to develop an innovative, independent research program that complements and enhances our existing strengths. Candidates with research interests in exciting areas of eukaryotic cell biology and using a variety of experimental approaches and systems are encouraged to apply. New faculty will be eligible to hold graduate school appointments in the Gerstner Sloan-Kettering Graduate School of Biomedical Sciences, the Weill Graduate School of Medical Sciences of Cornell University, as well as the Tri-Institutional MD/PhD Training Program. Sloan-Kettering has an outstanding infrastructure as well as state-of-the-art core resources, and we are now significantly expanding our research programs.

Interested individuals should e-mail their application, preferably in PDF format, to: **cellbio@mskcc.org** by November 15, 2007. The application should include a Curriculum Vitae, a description of past research, a description of proposed research, and copies of three representative publications. Candidates should arrange to have three signed letters of recommendation sent by e-mail to: **cellbio@mskcc.org** and by postal mail to: **Cell Biology Search, c/o Tiffany Lennon, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, Box 135, New York, NY 10065.** The letters should arrive by November 15, 2007. Inquiries can also be made by e-mail to: **cellbio@mskcc.org.** EOE/AA.

Memorial Sloan-Kettering Cancer Center
The Best Cancer Care. Anywhere.
www.mskcc.org

Faculty Positions in Molecular Biology

The Molecular Biology Program of the Sloan-Kettering Institute, Memorial Sloan-Kettering Cancer Center (www.ski.edu), has initiated a faculty search at the Assistant Member level (equivalent to Assistant Professor). We are interested in outstanding individuals who have demonstrated records of significant accomplishment and the potential to make noteworthy contributions to the biological sciences as independent investigators. Successful applicants will have research interests that move the Program into exciting new areas that complement and enhance our existing strengths in the areas of maintenance of genomic integrity, regulation of the cell cycle, and regulation of gene expression. Faculty will be eligible to hold appointments in both the Gerstner Sloan-Kettering Graduate School of Biomedical Sciences and the Weill Graduate School of Medical Sciences of Cornell University.

Candidates should e-mail their application in PDF format to: **molbio@mskcc.org by November 15, 2007.** The application should include a CV, a description of past research, a description of proposed research, and copies of three representative publications. Candidates should arrange to have three signed letters of reference sent by e-mail to: **molbio@mskcc.org** or by regular mail to **Dr. Kenneth Marians, c/o Steven Cappiello, Box 135, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, New York 10065.** The letters should arrive by November 15, 2007. Inquiries may be sent to Mr. Cappiello at: **molbio@mskcc.org** or to Dr. Kenneth Marians, Chair, Molecular Biology Program: **kmarians@sloankettering.edu.** Memorial Sloan-Kettering Cancer Center is an Equal Opportunity Employer. Smoke-free environment.

Memorial Sloan-Kettering Cancer Center
The Best Cancer Care. Anywhere.
www.mskcc.org

Tenure-Track Faculty Position in Biochemistry and Molecular Biology

We are seeking to fill a faculty position at the **ASSISTANT, ASSOCIATE OR FULL PROFESSOR** rank. Applicants at the Assistant Professor level must have a Ph.D. or equivalent with at least two years postdoctoral training. Applicants at the Associate or Full Professor level are further expected to have a strong record of research productivity and extramural support. All areas of biochemistry and molecular biology will be considered, but special consideration will be given to those whose research expertise complements existing faculty interests. These include neurobiology (including receptor trafficking and neurogenesis), regulation of protein synthesis and degradation, transcriptional regulation and chromatin silencing, cell signaling through protein kinases and phosphatases, DNA damage and repair, enzyme catalysis, molecular chaperones, and cancer biology (including chemopreventive action of retinoids, integrin signaling, invasive carcinoma, progression to metastatic disease, and gene therapy). Teaching responsibilities include participation in both medical and graduate school courses. The Department will assist with technical support and competitive start-up funds. LSUHSC-S maintains a central Research Core Facility encompassing eight state-of-the-art technologies.

Review of applications will begin in **November 2007**. Send *curriculum vitae*, a description of current and future research interests, and the names of three referees to: **Robert E. Rhoads, Ph.D., Professor and Head, Department of Biochemistry and Molecular Biology, Louisiana State University Health Sciences Center, 1501 Kings Highway, Shreveport, LA 71103; http://www.shrevebiochem.com/**

LSUHSC is an Affirmative Action Employer.

UK
UNIVERSITY OF KENTUCKY

Department of Microbiology, Immunology and Molecular Genetics Two Positions at the Assistant/Associate Professor Level

The Department of Microbiology, Immunology and Molecular Genetics, College of Medicine, University of Kentucky, seeks two tenure track faculty in **MICROBIAL PATHOGENESIS** at the Assistant or Associate Professor level. Areas of research interest include: host response to microbial pathogens, genetic basis of resistance to microbial infection, microbial virulence mechanisms, innate defenses against infection, and vaccine development. Applicants should have a Ph.D. and/or M.D., or equivalent degree, and postdoctoral experience. Successful candidates are expected to develop/maintain an innovative, externally funded research program as well as participate in graduate and medical student teaching. This is an excellent opportunity to join a department with strong predoctoral and postdoctoral training programs, and research in microbial pathogenesis, eukaryotic molecular biology, molecular and cellular immunology, and molecular virology. Excellent start-up funds, state-funded salary commensurate with experience and modern research facilities will be provided.

Applications should include curriculum vitae, representative reprints, a summary of past experience, a statement regarding research interests and future plans, as well as three letters of recommendation. All material should be sent to: **Chair, Faculty Search Committee, Department of Microbiology and Immunology and Molecular Genetics, MS409, Medical Center, University of Kentucky, Lexington, KY 40536-0298. Telephone: 800-462-5257; FAX: 859-257-8994; kfres1@pop.uky.edu**.

The University of Kentucky is an Equal Opportunity/Affirmative Action Employer and has an affirmative duty to reasonably accommodate otherwise qualified individuals with a disability.

MEDICAL COLLEGE OF WISCONSIN

Tenure Track Faculty Position in Developmental and Stem Cell Biology

Department of Cell Biology, Neurobiology and Anatomy/ Regenerative Medicine Program

A tenure track faculty position at the Assistant or Associate Professor level is available for a cell biologist who uses cellular and/or molecular-genetic approaches to address fundamental aspects of stem cell biology. Candidates applying knowledge of developmental biology to the study of human embryonic stem cell differentiation and/or pluripotency are particularly encouraged to apply. Competitive salary, laboratory space and start-up funds are available. Candidates at the Associate Professor level are expected to bring a vigorous research program with significant extramural funding. Current research strengths in the department include developmental biology of the gastrointestinal, cardiovascular and ocular systems. Candidates whose work complement these areas and incorporate innovative approaches are especially encouraged to apply. A Ph.D. or M.D./Ph.D. degree (or equivalent), plus additional postdoctoral experience are essential.

Interested individuals should send a resume, research plans, and the names of three references to:

Dr. Stephen A. Duncan
Chairman, Search Committee
Regenerative Medicine Program
Department of Cell Biology, Neurobiology and Anatomy
Medical College of Wisconsin
8701 Watertown Plank Rd
Milwaukee, Wisconsin 53226-0509

For more information on the MCW Cell Biology Department visit our Website at **http://www.mcw.edu/cellbio/**.

AA/EOE

DIRECTOR, CARDIOVASCULAR DISEASE RESEARCH PROGRAM

Applications are invited for an experienced scientist to direct the Cardiovascular Disease Research Program at North Carolina Central University (NCCU). The Program Director will have a unique opportunity to lead a multidisciplinary, inter-institutional cardiovascular disease research program located in the 40,000 sq ft. Julius.L. Chambers Biomedical/Biotechnology Research Institute (JLC-BBRI). This state-of-the-art facility, which also houses NCCU's Cancer Research and Neuroscience of Drug Abuse Programs, offers a range of research-related resources including Genomics, Bioinformatics, and Transgenic Zebrafish Core Facilities, and a modern animal care and use facility.

In addition to conducting and promoting cardiovascular research, the Program Director will provide scientific and administrative leadership for all JLC-BBRI cardiovascular disease research projects/programs. The Program Director will support existing cardiovascular disease research projects/programs as well as forge new partnerships with scientists at other institutions/corporations. The proximity of NCCU to the North Carolina Research Triangle Park and to the state's flagship research universities will afford the Director an unusually rich opportunity to develop joint programs in cardiovascular biology with a high probability for long-term success.

Applicants must hold a Ph.D. and/or M.D., have a record of sponsored research program management, and meet requirements for a tenure-track faculty appointment at the Associate Professor or Professor level in an NCCU basic science department. Additional requirements include demonstrated administrative and scientific leadership, a strong record of peer-reviewed cardiovascular research publications and research funding, prior teaching experience at the undergraduate and graduate levels, and other professional accomplishments. Review of applicants will begin immediately and will continue until the position is filled. Applicants should submit curriculum vitae, a description of research interests, and contact information for three references to: **Ms. Connie Key, Julius L. Chambers Biomedical/Biotechnology Research Institute, North Carolina Central University, 700 George Street, Durham, NC 27707; Email: chkey@nccu.edu.** For more information about the BBRI and NCCU visit **http://www.nccu.edu/BBRI**.

NCCU is a constituent institution of the University of North Carolina System and an Equal Opportunity, Affirmative Action Employer. NCCU complies with the Immigration Reform and Control Act of 1986.

MICHIGAN STATE UNIVERSITY

Faculty Position in Metabolic Regulation of Cellular and Tissue Function Department of Physiology

The Department of Physiology invites applications for a tenure-track appointment at the Associate/Full Professor level in metabolic regulation of cellular and tissue function. Areas of interest include, but are not limited to diabetes and obesity (metabolic syndrome, diabetic complications, epigenetic models); inflammation and cardiovascular disease; and neuronal control of metabolism. Candidates must hold a Ph.D., M.D., or equivalent degree as well as an established extramurally funded research program.

The successful candidate will join a MSU department with strong basic research programs in diabetic complications, ß-cell function, lipid metabolism, inflammation, neuroscience and biomedical imaging. He or she will be expected to interact collaboratively with other faculty in the department and university and participate in the departmental teaching mission. The laboratory is in a new building that offers state of the art research facilities including animal research, proteomics, genomics and confocal microscopy facilities, as well as library and teaching facilities.

Interested individuals should submit a complete curriculum vita, a brief statement of research interests, and electronic copies of key publications. Applicants should also provide the names and contact information of three individuals who can evaluate their accomplishments and future potential for research and teaching. Review of applications will begin September 30, 2007 and continue until the position is filled.

Applications should be sent electronically to: **pslfcpos@msu.edu, Chair, Metabolic Regulation Search Committee:William S. Spielman, Professor and Chairperson, Department of Physiology, Michigan State University, East Lansing, MI 488424-3320, Phone: 517-353-4539.**

Michigan State University is committed to achieving excellence through cultural diversity. The university actively encourages applications and/or nominations from women, persons of color, veterans and persons with disabilities.

MSU IS AN AFFIRMATIVE ACTION, EQUAL OPPORTUNITY EMPLOYER.

Harvard University

is recruiting tenure track faculty at the Assistant Professor level for a new multi-disciplinary **Department of Stem Cell and Regenerative Biology (DSCRB)**, Harvard's first joint Department bridging the Faculty of Arts and Sciences and the Medical School.

The department's research and teaching focus includes developmental biology broadly interpreted; stem and progenitor cell biology; tissue and organ formation; tissue regeneration, and repair– studied at the molecular, cellular, and organismic levels across organ systems. We are seeking faculty with a history of innovative, interactive research using human, other mammalian or non-mammalian systems and those with an interest in teaching undergraduate, graduate and/or medical students. Faculty will join a dedicated core of scientists and physician-scientists emphasizing stem cell and regenerative biology to inform the understanding of human diseases.

Applications including curriculum vitae, reprints of publications, statement of present and future research plans (1-3 pages), and three letters of recommendation should be submitted to Professors **Andrew McMahon** and **Kenneth Chien**, co-chairs, DSCRB Search Committee c/o **Raymond_Coderre@harvard.edu**. We strongly encourage applications from women and minority candidates. Submission by **October 31, 2007** is encouraged.

Harvard is an Affirmative Action/Equal Opportunity Employer.

ASSISTANT PROFESSOR

Massachusetts General Hospital Cancer Center and Harvard Medical School

The Massachusetts General Hospital Cancer Center is seeking applications for a tenure track faculty position at the level of Assistant Professor. We seek outstanding individuals who wish to establish a strong cancer research program with interests including, but not limited to, cancer biology, cancer genetics, genetic model organisms, signal transduction, and cell cycle checkpoints. Candidates must hold a Ph.D. and/or M.D. degree (or equivalent), have postdoctoral experience and a strong record of accomplishment in research. Applications from women and minority candidates are strongly encouraged.

Candidates should submit a curriculum vitae including a full list of publications and a brief statement of research and teaching interests to the address below. Four letters of reference should be mailed directly to the Search Committee.

Search Committee
c/o Carol Ann Hannan
MGH Cancer Center
13th Street, Building 149, Room 7204
Charlestown, MA 02129

Complete applications including four letters of reference must be received by **October 15, 2007**.

Massachusetts General Hospital and Harvard University uphold a commitment to Affirmative Action and Equal Opportunity.

UTMB
The University of Texas Medical Branch

FACULTY POSITIONS IN BIOINFORMATICS AT UTMB

The Sealy Center for Molecular Medicine (SCMM) and the Institute for Clinical and Translational Research (ICTR) at the University of Texas Medical Branch (UTMB) at Galveston are seeking outstanding applicants for three new positions in bioinformatics—a tenure-track professor, a tenure-track assistant or associate professor, and a postdoctoral fellow. Substantial startup packages are available for UTMB faculty positions.

Tenure-Track Professor (STAR Regents Research Scholar): Individuals with outstanding externally funded programs in bioinformatics are sought for this highly competitive professor position supported by the UT System STAR program. The successful applicant will take a leadership role in developing an interdisciplinary, inter-institutional effort in bioinformatics and systems biology. Scientists with interest in defining protein interaction networks, inference of network architecture and relationships, and integration with dynamical pathway modeling are specifically sought.

Tenure-Track Assistant or Associate Professor: Candidates for this assistant or associate professor position should have potential and interest in developing an extramurally funded program in the bioinformatics of protein interaction networks, pattern recognition statistics, and/or pathway modeling. The successful applicants will be jointly appointed in The Department of Biochemistry and Molecular Biology at a rank and salary commensurate with experience.

Postdoctoral Fellow (In Collaboration with Sandia National Labs): This postdoctoral fellow position will work in conjunction with an emerging inter-institutional collaboration between the SCMM and Sandia National Laboratories. The successful candidate will be involved in developing/analyzing stochastic models of inflammation-induced signaling networks and working with teams developing high-content imaging and computational mathematics.

A strong interdisciplinary collaborative environment is available with additional opportunities for interactions with investigators in centers of scientific excellence in aging, cancer, infectious diseases, structural biology and environmental health. Access to extensive computational resources are available at UTMB. UTMB is a member of the Houston/Galveston W.M. Keck Center for Interdisciplinary Bioscience Training and the Gulf Coast Consortium for Bioinformatics. To apply for any of these positions, please send a C.V., brief description of research interests and names of four references to: **Allan R. Brasier, MD, Director, Sealy Center for Molecular Medicine, The University of Texas Medical Branch, 301 University Blvd., Galveston, TX 77555-1060; Email: arbrasic@utmb.edu**.

UTMB is an Equal Opportunity/Affirmative Action University that proudly values diversity. Candidates of all backgrounds are encouraged to apply.

FACULTY POSITIONS

THE UNIVERSITY OF CALIFORNIA AT BERKELEY
Faculty Positions in Molecular and Cell Biology

The Department of Molecular and Cell Biology seeks applications for two faculty positions. We seek candidates with Ph.D. and/or M.D. degrees who have a strong interest in undergraduate and graduate teaching and demonstrated excellence, originality and productivity in research. Applications should include a curriculum vitae; a list of publications; a brief description of research accomplishments; a statement of research objectives and teaching interests; and reprints of three most significant publications. Please arrange to have three letters of reference sent in by the deadline date of November 15, 2007. Potential reviewers should be referred to the Statement of Confidentiality found at: **http://apo.chance.berkeley.edu/evalltr.html**. Successful candidates are expected to join the faculty July 1, 2008 or thereafter. On-line applications and letters of reference are preferred and can be made through **http://mcb.berkeley.edu**. Paper applications should be directed to:

Faculty Search [indicate preferred search area(s)]
Department of Molecular and Cell Biology
University of California at Berkeley
142 Life Sciences Addition #3200
Berkeley, CA 94720-3200

Eukaryotic Genetics/Genomics #1111

The Division of Genetics, Genomics and Development seeks applications for a faculty position at the level of Assistant Professor (tenure-track), in any area of genetics/genomics, with a preference for research in behavioral genetics or in human or mammalian variation, epigenetics or disease. Closing date for receipt of applications is **November 15, 2007**.

Biochemistry and Biophysics #918

The Division of Biochemistry and Molecular Biology seeks applications for a faculty position at the level of Assistant Professor (tenure-track). Excellent candidates in all areas of modern biochemistry and biological chemistry will be considered, but we are particularly interested in candidates who are applying quantitative tools to the study of biological macromolecules. Closing date for receipt of applications is **November 15, 2007**.

The University of California is an Affirmative Action/Equal Opportunity Employer; these are nine-month academic year appointments.

Group Leaders

Reference number: PI/07/15

Paterson
Institute for Cancer Research

Group Leader positions are available in the Paterson Institute, a leading cancer centre of excellence core-funded by Cancer Research-UK, the largest independent cancer research organisation in the world. The Institute supports numerous basic and translational cancer research programmes (see our website) and is located adjacent to the Christie Hospital, a specialist cancer hospital, thereby ensuring ample opportunities for interaction across the basic to clinical research spectrum. The Institute is also at the heart of the newly formed Manchester Cancer Research Centre (MCRC) - www.manchester.ac.uk/mcrc

The positions are open to non-clinical and clinical researchers. Substantial core research support will be provided, including fully-funded positions, start-up and running costs as well as access to a wide-range of state-of-the-art research services. Positions are for six years initially with consideration for promotion to Senior Group Leader after five years. Direct appointment to a senior position will also be considered.

You would be expected to develop an independent research programme in an area of cancer biology that complements the overall research efforts of the Institute and the MCRC. We are particularly interested in programmes within the areas of:

- Tumour microenvironment
- Mammalian cell proliferation and cell signalling
- Genome instability
- Mouse cancer models

Informal enquiries should be addressed to Prof Nic Jones, Director of the Institute, email: njones@picr.man.ac.uk and applications including a CV, names of three referees and a short summary of past research and future plans should be sent to Laura Humes, HR Assistant, email: lhumes@picr.man.ac.uk

The deadline for receipt of applications is Friday 26 October 2007

www.paterson.man.ac.uk

MANCHESTER 1824
The University of Manchester

CANCER RESEARCH UK

Department of Health and Human Services
National Institutes of Health
National Cancer Institute

The Cell and Cancer Biology Branch at the National Cancer Institute is currently investigating various aspects of normal tissue stem cells, as well as the microenvironment-tumor relationship. This area of cancer research holds great promise in the treatment and prevention of cancer and a great deal remains to be learned about the identification and isolation of these cells. We are accepting applications for a Staff Scientist position. Incumbent will oversee the research activities of this Branch and specifically our efforts in defining the role of stem cells as a cancer initiator and determinant of the metastatic process. The applicant will have an MD or Ph.D. in biomedical science and a demonstrative record of strong leadership in addition to working in a collaborative setting. The salary range will be $74,503 - $162,371.

The Cancer and Cell Biology Branch (CCBB) is part of the Center for Cancer Research (CCR), which is the largest organization at the NCI dedicated to conducting basic, translational and clinical research on the discovery of the causes and mechanisms of cancer. The CCR is a highly interactive, interdisciplinary group of researchers who have access to new technology and the ability to participate in clinical investigations while maintaining a foundation for independent research.

As part of the Department of Health and Human Services (DHHS), which oversees the biomedical research programs of the National Institutes of Health and those of the NIH's research Institutes, NCI offers a vast array of resources and exciting opportunities for interlaboratory collaboration to our investigators. The NCI/NIH intramural research program provides an exceptionally rich environment for career development. Please send or email CV, cover letter and three references to: **Simone John, Office of the Director, National Cancer Institute, 31 Center Drive, Room 11A19, Bethesda, MD 20892 or johnsi@mail.nih.gov**. All applications must be submitted no later than **October 15, 2007**.

Senior Medical Officer

The Division of Extramural Research (DER), National Institute of Dental and Craniofacial Research (NIDCR) seeks an experienced, highly qualified Senior Medical Officer with expertise in infectious diseases, pharmacovigilance, and product development. The Division of Extramural Research, NIDCR, is responsible for all extramural research in the Institute. This ranges from basic through translational to clinical research, including large and complex Phase III efficacy trials as well as population based trials in the dental-practice based research networks, and health disparities centers. Product development activities include development and clinical evaluation of diagnostics, vaccines and therapeutics across the spectra of microbiology, immunology, mineralized tissue, salivary gland physiology and dysfunction, neurosciences, head and neck cancer, developmental biology, regenerative medicine, tissue engineering and materials science.

The incumbent will serve as key advisor to the Director DER and the scientific programs on all clinical research issues and provide objective, experience-based guidance and oversight; be responsible for oversight of the DER clinical research program including development, standardization, implementation and execution of policies, procedures and standards of conduct for clinical research to ensure that all DER, NIDCR-sponsored domestic and international clinical research is conducted in full compliance with all applicable regulations and policies and meets established standards of quality, integrity and ethics; be responsible for identifying and resolving a variety of complex clinical trials management, policy and administrative issues that require close coordination and interfacing within the DER clinical program, with NIH Institutes, CDC, the DoD, the FDA, other Federal agencies, as well as pharmaceutical companies and patient advocacy and community groups; assume responsibility for designing, implementing and overseeing all safety oversight activities associated with clinical research comprising more than minimal risk to the human subjects, including all interventional trials and clinical studies in vulnerable populations; e.g., pediatrics, pregnant women; manage and oversee the DSMBs overseeing the Phase III clinical trials and interfacing with counterpart physicians associated with the trials, in industry and at the FDA; and serve as the physician interfacing on medical and safety issues with medical colleagues affiliated with clinical research supported by NIDCR.

Applicants must have a MD degree and be Infectious Diseases Board eligible or certified. In addition, specific clinical expertise in the current state of product development and clinical trials and practice in infectious diseases is required along with a broad understanding of the policies and programs necessary for a federally-funded clinical research program. Women and minorities are encouraged to apply. Salary commensurate with qualifications and experience.

Applicants should submit a current CV, Bibliography and the names and contact information for three references to **Ms. Carol Beasley, National Institute of Dental and Craniofacial Research, 31 Center Drive, MSC 2290, Bldg. 31, Room 2C-39, Bethesda, MD 20892-2290**. Applications also may be submitted via email to **carol.beasley@nih.gov**. The application deadline is **October 15, 2007**.

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Recognized worldwide for our cutting-edge medical and scientific research, the National Institute of Allergy and Infectious Diseases (NIAID) has a responsibility to improve global health in the 21st century. Our basic and applied research programs are aimed at improving diagnosis, treatment, and prevention of immunological, allergic, and emerging and re-emerging infectious diseases.

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Applicants must hold a PhD or equivalent doctoral-level degree in any physical, biological, medical/health, or social/behavioral science, or any engineering discipline. Individuals with a master's degree in engineering and three years of post-degree professional experience also may apply. Federal employees are not eligible and U.S. citizenship is required.

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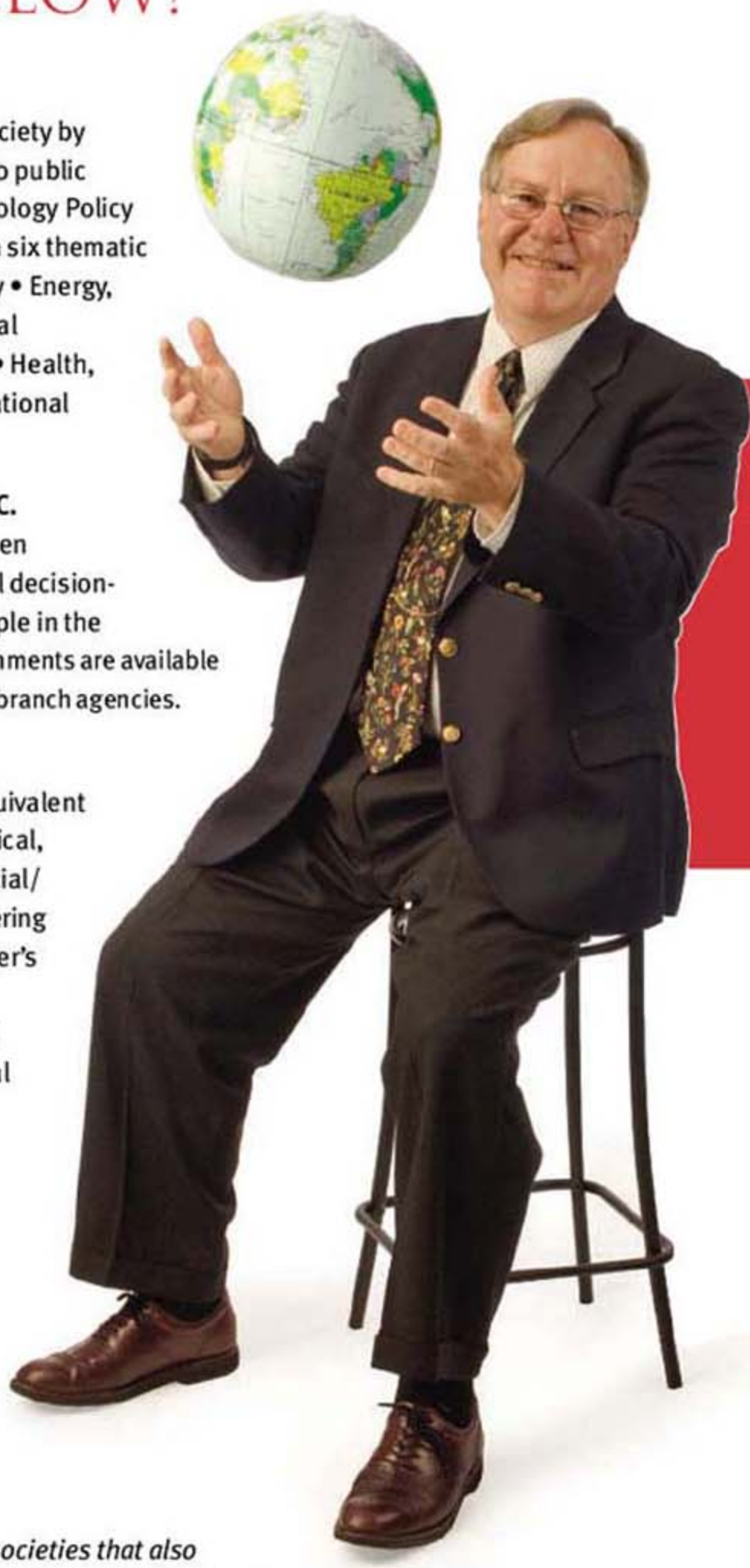
The application deadline for the 2008-2009 fellowships is 20 December 2007. Fellowships are awarded in the spring and begin in September. Stipends range from $67,000 to $87,000.

AAAS partners with 30 scientific societies that also sponsor congressional and executive branch fellowships. Visit our Web site for more details. fellowships.aaas.org



Enhancing Public Policy, Advancing Science Careers

James Fleming, PhD

History of Science, Princeton University.

2006-2007 AAAS Roger Revelle Fellow in Global Stewardship, serving as a public policy scholar at the Woodrow Wilson International Center for Scholars.

Recently returned to Colby College, where he serves as professor of Science, Technology, and Society.

AAAS
ADVANCING SCIENCE. SERVING SOCIETY

Up to three research fellowship positions are available in a new international joint initiative, funded by the Human Frontiers Science Program. The collaborators include Peter MacCallum Cancer Centre and Swinburne University in Australia and University of California Berkeley, USA. The initiative will involve the application of advanced imaging techniques to determine how cell polarity proteins regulate thymocyte development using both *in vitro* and *in vivo* approaches. The individual research fellows will each be associated with a single institution but will interact with researchers at the other institutions to apply multidisciplinary approaches to the study. Experience in immunology, cell biology and photonics is required, and the successful candidates will have demonstrated skills in both independent research and working within a team. The positions are available for one year in the first instance, but renewable for up to three years thereafter.

Interested candidates should send a copy of their *curriculum vitae* to either:

Sarah Russell, Peter MacCallum Cancer Centre
(sarah.russell@petermac.org)

Ellen Robey, UC Berkeley
(erobey@berkeley.edu)

or

Min Gu, Swinburne University of Technology
(mgu@swin.edu.au)

EMBL EMBL-EBI

Part of the European Molecular Biology Laboratory (EMBL), the European Bioinformatics Institute (EBI) is located on the Wellcome Trust Genome Campus at Hinxton, near Cambridge and provides cutting-edge research, service and training in the field of bioinformatics. The EBI, a vibrant and multicultural science institute, is looking for a

Team Leader

Macromolecular Database Group, United Kingdom

We seek to appoint a Team Leader for the 3D Macromolecular Structure Database (MSD) at the EMBL-EBI (see: www.ebi.ac.uk/msd). This person will be responsible for an ambitious programme, which is part of the worldwide Protein Databank (wwPDB), and integrates with the other research and service activities of the EMBL-EBI. The MSD is the European Project for the collection, management and distribution of data on macromolecular structures. It is a member of the worldwide Protein Databank which maintains the global PDB archive of 3D biological structural data. The MSD databases serve a worldwide community of scientists through a web site built on data warehouse technologies and through software and hardware that facilitates integration and access.

The post holder will be responsible for strategic leadership and development of the European infrastructure services for macromolecular structure data and their relationship to related activities throughout the world. The team currently includes 23 staff, with responsibility for data curation and data services, as well as the associated development of software and database systems to maintain and provide the data users. This includes the production of novel and powerful search tools.

Candidates are expected to be experienced scientists with expertise in structural biology and software development. We would expect them to have an international reputation built on demonstrated competence in the leadership of complex international projects. The Team Leader will also be expected to apply for grant funding to enable future development of the team and may also pursue a research programme in the analysis of structural data.

Informal enquiries would be welcomed and should be addressed to Professor Janet Thornton (director@ebi.ac.uk).

For further information please see our websites: www.ebi.ac.uk and www.embl.org

Closing date: 5 November 2007

EMBL is an inclusive, equal opportunity employer offering attractive conditions and benefits appropriate to an international research organisation.

To apply, please send a CV (including names and addresses of three referees) and an outline of a vision for the development of the PDB at the EBI (candidates interested in research should also submit a research plan) by email, quoting ref. no. S/07/132 in the subject line, to: applications@ebi.ac.uk

www.embl.org
www.ebi.ac.uk

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- Applicants should be recognized as national/international authorities and should have planned and executed difficult programs of national significance that show outstanding attainment in their field of research.
- Optional Application for Federal Employment (OF-612), Application for Federal Employment (SF-171), or resume, along with technical qualifications and Executive Core Qualifications (ECQs) must be received by 30 September 2007. In order to receive full consideration, all technical qualifications and ECQ's must be discussed in detail.
- Apply to: **Naval Research Laboratory, Code 1810GK, Announcement #NW7-XXXX-00-K9711724-SES, 4555 Overlook Avenue SW, Washington, DC 20375-5320.** Faxed or emailed applications will not be accepted. To view full vacancy announcement and/or to apply online visit **https://hro1.nrl.navy.mil/jobs/index.htm**.
- For further information contact Ginger Kisamore, Human Resources Office, NRL at **ginger.kisamore@nrl.navy.mil** or **(202) 767-3792**.

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Research Scientist I / II

Biology Dept.
Foster City, CA

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The candidate must have substantial working knowledge of protein purification methods development, optimization and troubleshooting. He or she will be expected to conduct active lab work independently and with RAs. Knowledge of protein biophysics and/or molecular biology basics is a plus. Requires a PhD in Biochemistry/Molecular Biology or related discipline with two to four years of working experience with recombinant protein purification and characterization in academic and/or industrial setting.

Other requirements:

- Technically proficient in use of AKTA instruments, diverse range of column chromatography and general laboratory protein biochemistry procedures.
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- Must be able to independently analyze results and present data.
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PRINCIPAL SCIENTIST – JOB #IND070456

In this vital role, you'll oversee the resources of our technical affairs group, which includes validating new products and processes, directing technical investigations, and developing and implementing process improvements. To qualify, you must have either an MS in Science with 6 years of laboratory experience or a Ph.D with 4 years, and knowledge of chemical and immunological manufacturing processes.

PRODUCT SUPPORT SCIENTIST – JOB #IND070518

As a member of our technical affairs group, you'll perform validation of new products and processes, conduct technical investigations of non-conforming products, and implement process improvements. To qualify, you must have either a BS in Science with 5 years of experience, an MS with 3 years or a Ph.D, and knowledge of statistics and analytical chemistry and instrumentation.

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Max Planck Institute for Demographic Research

The Max Planck Institute for Demographic Research (MPIDR) seeks to recruit a

Research Scientist

to conduct research for the Laboratory of Demographic Data. Qualified demographers, sociologists, statisticians, and other scientists with a research background in the social sciences are invited to apply. We intend to fill the position as soon as possible. The duration of the contract will initially be limited to three years. The salary is paid according to qualification and in accordance with the rules of federal employees in Germany, up to level 14 TVöD.

The successful applicant must have completed a Ph.D. degree in demography or a related field. He or she must have a proven record of scientific work and theoretical experience in the field of fertility and its determinants in Europe and other industrialized societies as well as knowledge of the relevant literature.

The candidate will in the main process and analyze population and survey data on fertility. The position requires expertise in statistical and demographic analyses and practical skills in handling demographic data. Fluency in English is essential

The Max Planck Society is committed to employing handicapped individuals. The Society wishes to increase the share of women researchers.

Applications should include a CV with a statement of academic interests and relevant experience, a list of publications, two recommendations, and contact details of two referees.

Please send all materials **by 21st October 2007** to the:

Max Planck Institute for Demographic Research
Attn. Edelgard Katke
Konrad-Zuse-Str. 1, 18057 Rostock, Germany
Email: katke@demogr.mpg.de

MAX-PLANCK-GESELLSCHAFT

TEXAS HEART® INSTITUTE
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The Texas Heart Institute (THI) at St. Luke's Episcopal Hospital, affiliated with the University of Texas Health Science Center at Houston is establishing a premier Cardiovascular Stem Cell Biology Research Center. We are currently recruiting established and promising investigators who have established records of independent and innovative research in Cardiovascular Stem Cell Biology. The positions offer very attractive recruitment packages and excellent opportunity for translational and collaborative research using state of the art facilities in a rich academic environment within one of the world's largest medical centers.

Please e-mail all inquiries, CVs and letters of references to:

Ms. Sarah Cuddy
Administrative Assistant
Center for Cardiovascular Genetic Research
Texas Heart Institute at St. Luke's Episcopal Hospital
Sarah.Cuddy@uth.tmc.edu

Post-Doctoral Position
Cellular and Molecular Regulation of Angiogenesis and Vascular Regression

Principal Investigator:
Roberto Nicosia, MD, PhD

Candidate will have up to three years of post-doctoral experience, and a strong background in cell and molecular biology. Desired background includes vascular biology, extracellular matrix biology, and immunology. Position is in the Department of Pathology, University of Washington/VA Medical Center, Seattle, WA

Send your CV and cover letter electronically to:
nicosialab@gmail.com
or by post to:
Eric Fogel
1660 S. Columbian Way
Mailstop S-151
Seattle, WA 98108

FACULTY POSITIONS

Washington University in St. Louis
SCHOOL OF MEDICINE

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DEPARTMENT of CHEMISTRY
Biochemistry

The Department of Chemistry in the College of Arts and Sciences at American University seeks a full-time tenure-track faculty member at the rank of **ASSISTANT PROFESSOR** for academic year 2008-2009. The successful candidate must have a Ph.D. in chemistry and be able to show evidence of strong teaching skills. Primary teaching responsibilities include biochemistry and organic chemistry. Applicants are expected to maintain a strong research record. Other responsibilities also include supervising graduate and undergraduate research students and mentoring both undergraduate and graduate students. To apply, submit a letter of application, curriculum vitae, a statement of research interests, and a research plan, and arrange to have three letters of reference sent directly from individuals who are able to comment on the applicant's teaching and research skills to: **Dr. Albert Cheh, Department of Chemistry, American University, 4400 Massachusetts Avenue N.W., Washington, DC 20016-8104; e-mail: acheh@american.edu; fax: 202-885-1752.** E-mail submissions are encouraged. American University is seeking highly dedicated teachers and scholars who are deeply committed to interdisciplinary learning, the application of new technologies in teaching and scholarship, and to the preparation of students for life in a diverse and rapidly changing global society. *Women and minority candidates are strongly encouraged to apply. American University is an Affirmative Action/Equal Opportunity Employer.*

The Amherst College Department of Chemistry (**website: http://www.amherst.edu/~chemistry/**) invites applications for a full-time tenure-track **ASSISTANT PROFESSORSHIP** in biochemistry or bio-organic chemistry beginning in July 2008. The position requires a Ph.D., and calls for teaching at the introductory and advanced undergraduate levels. Opportunities for teaching in interdisciplinary courses and programs are also available. The successful candidate will be expected to establish a vigorous research program in which undergraduates can substantively participate. The research program may span the boundaries between biochemistry and other sciences. Applicants should submit curriculum vitae, undergraduate and graduate transcripts, a statement of teaching philosophy, and a detailed description of their research plans, and should arrange for the forwarding of three letters of reference, all to: **Professor Joseph N. Kushick, Chair, Department of Chemistry, Amherst College, Amherst, MA 01002.** Review of materials will begin October 8, 2007.

Amherst College is a private, liberal arts institution of some 1,600 students and 190 faculty. Located in the Connecticut River Valley of western Massachusetts, it participates with Hampshire, Mount Holyoke, and Smith Colleges, and the University of Massachusetts in the Five-College Consortium. The College enrolls students from nearly every state and from more than forty countries.

Amherst College is an Equal Opportunity, Affirmative Action Employer and encourages women, persons of color, and persons with disabilities to apply. The administration, faculty, and student body are committed to attracting qualified candidates from groups currently underrepresented on campus.

POSITIONS OPEN

BACTERIAL PATHOGENESIS

POSTDOCTORAL FELLOW POSITION is available immediately to join the collaborative research groups of **Drs. David N. McMurray and Jeffrey D. Cirillo** studying tuberculosis pathogenesis. Selected individual will be primarily responsible for conducting independent research on mycobacterial pathogens and publication of results. Research will emphasize the molecular, cell biological and immunological characterization of virulence determinants in mycobacteria and their interactions with the host in a guinea pig virulence model. Ph.D. required and a record of productive experience in molecular biology of bacterial pathogens preferred. Send curriculum vitae and names and addresses of three references postmarked by October 31, 2007 (or until a suitable candidate is found), to: **Dr. Jeffrey D. Cirillo, Department Microbial and Molecular Pathogenesis, Texas A&M University Health Science Center, M.S. 1114, 471 Reynolds Medical Building, College Station, TX 77843-1114. Fax: 979-845-3479; e-mail: jdcirillo@medicine.tamhsc.edu.** Contact **Dr. Cirillo, telephone: 979-458-0778** for additional information.

Texas A&M University System Health Science Center is an Affirmative Action/Equal Opportunity Employer and encourages applications from women and minorities.

POSTDOCTORAL POSITIONS
Prostate Cancer

An excellent opportunity for career development to instructor and junior faculty appointment, the position will study the development and growth of prostate cancer using mouse prostate stem cell models. Focus will be on the role of the Pim protein kinase and regulation of TOR. Individuals should have a strong background in transgenic/knockout mouse models and molecular biology/protein chemistry. Forward curriculum vitae and the name of three references to: **Andrew S. Kraft, M.D., Director Hollings Cancer Center, 86 Johnathan Lucas Street, P.O. Box 250955, Charleston, SC 29425. E-mail: hccjobs@musc.edu.** Please reference ad #5001.

FACULTY POSITIONS

The UNIVERSITY of TEXAS SOUTHWESTERN MEDICAL CENTER at DALLAS

The Department of Internal Medicine/Division of Nephrology seeks an **ASSISTANT/ASSOCIATE PROFESSOR** for our expanding dialysis, transplantation, and clinical/translational research programs. Applicant must have an M.D. degree or equivalent from an approved Liaison Committee on Medical Education medical school and satisfactory completion of an internal medical residency and a nephrology fellowship from an Accreditation Council for Graduate Medical Education–accredited program. Level of appointment will be commensurate with experience. Candidate must be eligible for Texas medical licensure and be Board certified/eligible in Internal Medicine. We are recruiting both **CLINICIANS and CLINICAL SCHOLARS.** Duties of Clinician will include patient care with emphasis on dialysis and transplantation; Clinical Scholars will be expected to develop independent research programs and participate in our newly funded O' Brien Kidney Research Core Center. Duties will also include the teaching and training of medical students, graduate students, house staff, and fellows. Individuals who are eligible for our Disease-Oriented Clinical Scholars (DOCS) Program are particularly encouraged to apply. Visit our **website: http://www.utsouthwestern.edu/nephrology.** Send curriculum vitae, description of research interests, and three reference letters to: **Robert Toto, M.D., Director of Clinical Nephrology, University of Texas Southwestern, 5323 Harry Hines Boulevard, Dallas, TX, 75390-8856. E-mail: robert.toto@utsouthwestern.edu.**

UT Southwestern is an Equal Opportunity/Affirmative Action Employer.

FACULTY POSITIONS

TENURE-TRACK ASSISTANT PROFESSOR
Cell Biology
Brandeis University

The Brandeis Biology Department is seeking to fill a tenure-track position in the broad area of cell biology, beginning fall 2008. Areas of interest include cell polarity and structure, macromolecular assemblages, organelles, membrane systems and transport, cell division, cytoskeleton, cell motility, and cell adhesion. We are looking to complement existing strengths at Brandeis in cell and structural biology, development and function of the nervous system, chromosome structure and function, and biophysics. We expect that the appointment will be made at the **ASSISTANT PROFESSOR** level, although an appointment for more advanced candidates with exceptional qualifications may be considered. Candidates should have a Ph.D., M.D., or both, as well as postdoctoral experience. First consideration will be given to applications received by November 1, 2007. Candidates must submit initial information online at **website: http://www.bio.brandeis.edu/facultySearch/appFormMB.php.** Applicants should submit (preferably in PDF format) curriculum vitae, research plan, and publications, and should arrange for three letters of recommendation to be submitted to **e-mail: volencenter@courier.brandeis.edu.** *Brandeis University is an Equal Opportunity Employer, committed to building a culturally diverse intellectual community and strongly encourages applications from women and minorities.*

The UNIVERSITY of TEXAS SOUTHWESTERN MEDICAL CENTER at DALLAS

The Department of Internal Medicine, Division of Nephrology, seeks faculty at the **ASSISTANT/ASSOCIATE PROFESSOR** level who will develop independent research programs in kidney biology and disease. Individuals with expertise in human genetics or glomerular biology and who are eligible for Endowed Scholars or Disease-Oriented Clinical Scholars Programs are particularly encouraged to apply. Preference will be given to Physician-Scientists, but Basic Scientists will also be considered. Successful candidates will participate in our newly funded O'Brien Kidney Research Core Center. Applicant must have an M.D. or Ph.D. degree. Clinical duties, if applicable, include patient care activities in nephrology. Other responsibilities will include the teaching and training of medical students, graduate students, house staff, and fellows. Visit our **website: http://www.utsouthwestern.edu/nephrology.** Send curriculum vitae, description of research, and three reference letters to: **Peter Igarashi, M.D., Chief of Nephrology, University of Texas Southwestern, 5323 Harry Hines Boulevard, Dallas, TX 75390-8856. E-mail: peter.igarashi@utsouthwestern.edu.** *UT Southwestern is an Equal Opportunity/Affirmative Action Employer.*

MICROBIOLOGY FACULTY POSITION. The Department of Biology at Clark University, Worcester, Massachusetts **(website: http://www.clarku.edu/departments/biology/)** invites applications for a tenure-track appointment at the rank of **ASSISTANT PROFESSOR,** to begin fall 2008. The successful candidate will be expected to develop an externally funded research program in any area of microbiology involving Ph.D. and undergraduate students. The candidate will teach microbiology and other appropriate courses. Applicants should submit curriculum vitae, summary of research and teaching interests, and three publications. Three letters of reference should be received by the **Search Committee** prior to October 15, 2007, for full consideration **(e-mail: micro@clarku.edu).** Please see **website: https://www.clarku.edu/offices/hr/jobsdb.cfm?id=376&viewjob=1&grouping=F** for full position description. Inquiries may be directed to **e-mail: sfoster@clarku.edu.** *Affirmative Action/Equal Opportunity Employer. Minorities and women are especially encouraged to apply.*

POSITIONS OPEN

The NEUROSCIENCES INSTITUTE
La Jolla, California
Neural Modeling

Research positions are available to work with a diverse team using and developing autonomous robotic devices whose behavior is guided by large-scale neuronal networks (brain-based devices). Positions are available immediately at the **POSTDOCTORAL or ASSISTANT PROFESSOR** level. Applicants should have a background in areas such as modeling of complex neural systems or experimental systems neurophysiology. Experience with advanced computational techniques is desirable.

The Neurosciences Institute provides opportunities for interactions among researchers in various disciplines using both theoretical and experimental approaches with the overall goal of increasing fundamental understanding of brain function.

Interested candidates should send curriculum vitae including the names of three references to: **Dr. W. Einar Gall, Research Director, The Neurosciences Institute, 10640 John Jay Hopkins Drive, San Diego, CA 92121** or to **e-mail: job1@nsi.edu.**

The Neurosciences Institute is an Equal Opportunity Employer.

POSTDOCTORAL RESEARCH POSITIONS
Center for the Physics of Information
California Institute of Technology

The Center for the Physics of Information at the California Institute of Technology will have Postdoctoral Scholar positions available beginning in September 2008. Researchers interested in all aspects of the interface between information science and physical science are invited to apply. Please apply online at **website: http://www.ist.caltech.edu/joinus/positions.html#postdoc.**

Electronic copies of your curriculum vitae, publication list, statement of research interests, and three letters of recommendation are required. The deadline for receipt of all application materials is December 17, 2007.

The California Institute of Technology is an Equal Opportunity/Affirmative Action Employer. Women, minorities, veterans, and persons with disabilities are encouraged to apply.

POSTDOCTORAL RESEARCH POSITIONS
Institute for Quantum Information
California Institute of Technology

The Institute for Quantum Information at the California Institute of Technology will have Postdoctoral Scholar positions available beginning in September 2008. Researchers interested in all aspects of quantum information science are invited to apply. Please apply online at **website: http://www.iqi.caltech.edu.** Electronic copies of your curriculum vitae, publication list, statement of research interests, and three letters of recommendation are required. The deadline for receipt of all application materials is December 17, 2007.

The California Institute of Technology is an Equal Opportunity/Affirmative Action Employer. Women, minorities, veterans, and persons with disabilities are encouraged to apply.

A motivated **POSTDOCTORAL RESEARCHER** in computational structural biology is wanted to develop a TBM protein structure prediction algorithm in the Tsai group at Texas A&M University in the Biochemistry/Biophysics Department **(website: http://tsailab.tamu.edu).** Start date as soon as possible, since participation in CASP 8 is involved. Required skills are: background in the biological sciences as well as familiarity with UNIX/Linux, scripting, and programming. Pay based on the current NIH scale for postdoctorates. Please send (1) curriculum vitae, (2) three publications, and (3) three references to **e-mail: juanitaw@tamu.edu.**

POSITIONS OPEN

Three **POSTDOCTORAL POSITIONS** available immediately at the Hormel Institute, University of Minnesota (UMN), Section of Cancer Biology, Austin, Minnesota, for persons with doctoral training in cancer molecular or cell biology, biochemistry, angiogenesis, medicinal chemistry, sex steroid hormone signaling to investigate mechanisms of cancer chemoprevention and therapy by selenium and other agents. Working experience in recombinant DNA techniques, RNAi, apoptosis, autophagy, cell cycle regulation, angiogenesis, transgenic adenocarcinoma of mouse prostate, and other transgenic cancer models is highly desirable. If interested, please apply online at the UMN Employment Home Page **website: http://www.umn.edu/ohr/employment** and refer to requisition number 148039. Please send curriculum vitae also to: **Prof. Johnny Lu, e-mail: jlu@hi.umn.edu.** *The University of Minnesota is committed to the policy that all persons shall have equal access to its programs, facilities and employment without regard to race, color, creed, religion, national origin, sex, age, marital status, disability, public assistance status, veteran status, or sexual orientation.*

MARKETPLACE

Saluting the next generation of scientific leaders

CONGRATULATIONS to the 2007 UNCF/Merck Science Initiative Fellows

For the past 12 years, Merck & Co., Inc. has proudly partnered with United Negro College Fund (UNCF) to support the advancement of African Americans into biomedical professions to achieve the complementary goals of national economic competitiveness and social diversity. The UNCF/ Merck Science Initiative is pleased to congratulate this year's 36 scholarship and fellowship recipients -- undergraduate, graduate and postdoctoral students from 32 academic institutions across the United States.

The 2007 Fellows exemplify limitless potential as tomorrow's research scientists, professors and teachers. We applaud our award recipients – past and present – whose hard work and commitment represent the future of science and education.

For more information about the UNCF/ Merck Science Initiative, please visit: www.uncf.org/merck

I. Undergraduate Science Research Scholarship Awards

Nicole Bowles, New York University
Elijah Burbank, University of Washington
Charles Drummer, University of Delaware
Brandi Johnson, North Carolina A&T State University
Geron Johnson, Saginaw Valley State University
Paul Kelley, The Catholic University of America
Threshia Malcolm, Mount Holyoke College
Adriana Martin, Bloomfield College
Khadijatou Njimoluh, University of Maryland, Baltimore County
Emily Nwakpuda, North Carolina Central University
Arie Shaw, Xavier University
Delia Shelton, Southwestern University
Shayla Shorter, University of Maryland, Baltimore County
Rosa Wright, Albany State University

II. Graduate Science Research Dissertation Fellowship

Catherine Bangeranye, The Graduate Center, City University of New York
Clarisa Buckner, Yeshiva University
Courtney Goodwin, Johns Hopkins University
Rochelle Jean-Jacques, University of California, San Diego
Carl Johnson, University of Pittsburgh
Tori Matthews, University of Alabama, Birmingham
Winnette Mcintosh Ambrose, Johns Hopkins University
Johnnie Moore, Saint Louis University
Odi Osonkie, University of California, Los Angeles
Jocelyn Reader, University of Maryland, Baltimore
Tanya Russell, University of Colorado, Denver
Monica Sylvain, Louisiana State University, Baton Rouge

III. Postdoctoral Science Research Fellowship

Anthony Baucum, II, Vanderbilt University
Namandje Bumpus, University of Michigan
Michael Bernard Duncan, II, Harvard University
Erica Glasper, Princeton University
Lori Norton, Georgia Institute of Technology
Manu Platt, Massachusetts Institute of Technology
David Pride, Stanford University
Kimberly Raines, University of North Carolina, Chapel Hill
Christopher Williams, Tulane University
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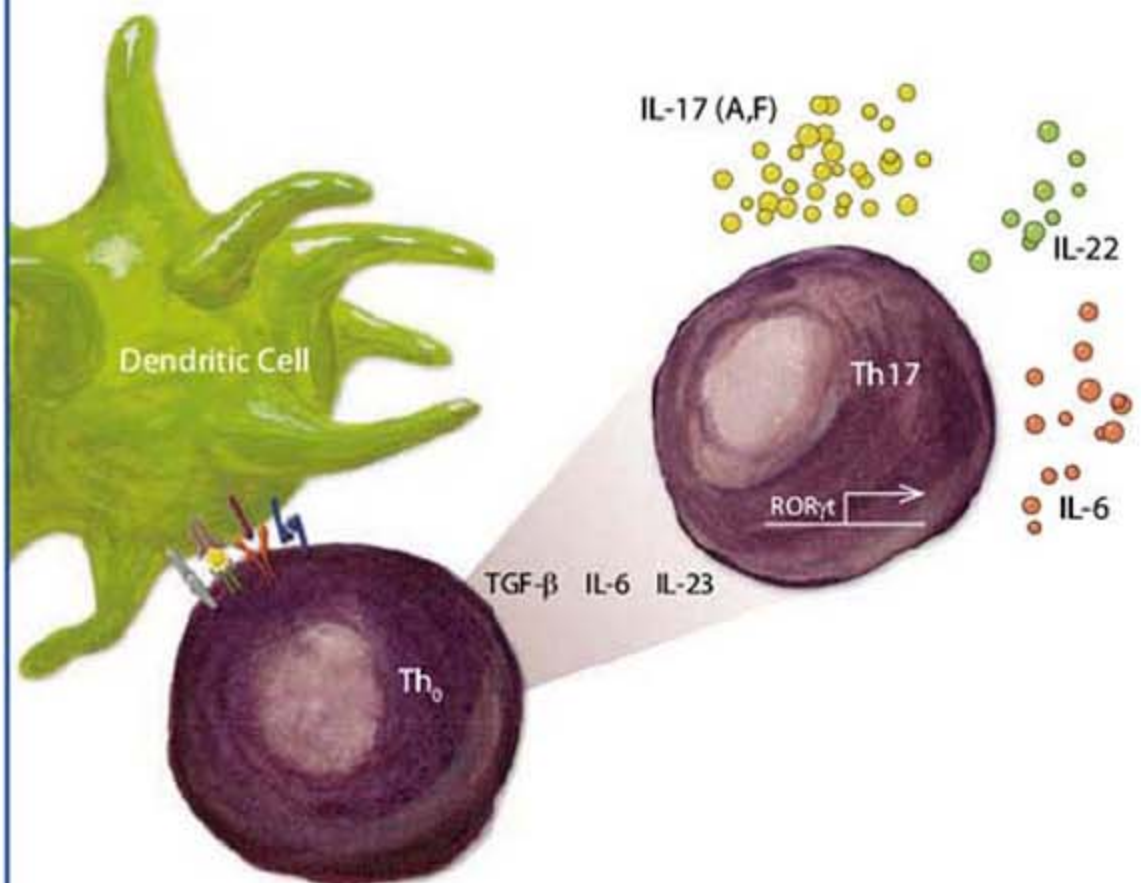
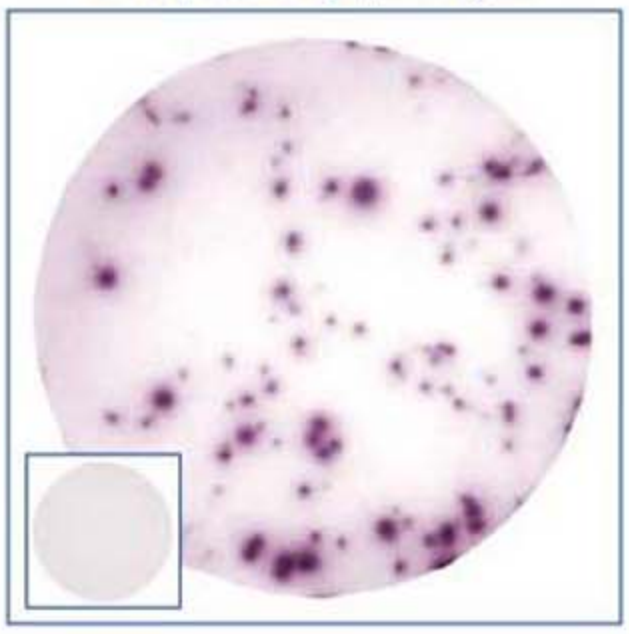


ELISpot Detection of
IL-17-producing Splenocytes



Mouse splenocytes (10^5 cells per well) were cultured in the absence (inset) or presence of PMA and a calcium ionophore. The frequency of IL-17 producing cells was measured with the mouse IL-17 ELISpot Kit (Catalog # EL421).

Th17-RELATED PRODUCTS

Molecule	Antibodies	Proteins	ELISAs/ Assays
CTLA-4	H M	H M	
EDG-1	H		
IL-6	H M R Ca CR E F P	H M R Ca CR E F P	H M R Ca P
IL-17	H M	H M	H M
IL-17 R	H M	H M	
IL-17 F	H M	H M	H M
IL-17 RC	H M	H M	
IL-22	H M	H M R	H M R

Molecule	Antibodies	Proteins	ELISAs/ Assays
IL-22 R	H	H	
IL-23	H M	H M R	
IL-23 R	H M	H M	
IL-27	H M	H M	M
RORγ	H		
STAT3	H M R		
TGF-β1	H	H M P	H M R Ca P
TRAF6	H		

Key: Ca Canine CR Cotton Rat E Equine F Feline H Human M Mouse P Porcine R Rat

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